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Dossier zur Nutzenbewertung gemäß § 35a SGB V

Fruquintinib (FRUZAQLA®)

Takeda GmbH

Modul 4 A, Anhang 4-G

Behandlung von Patienten mit metastasierendem Kolorektalkarzinom (mCRC), die zuvor mit verfügbaren Standardtherapien, einschließlich Fluoropyrimidin-, Oxaliplatin- und Irinotecan-basierten Chemotherapien, Anti-VEGF-Arzneimitteln und Anti-EGFR- Arzneimitteln, behandelt wurden und bei denen die Erkrankung unter Behandlung mit Trifluridin-Tipiracil oder Regorafenib fortgeschritten ist, oder die diese Behandlung nicht vertragen

Zusatzanalysen

Stand: 03.06.2024

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Studie FRESCO-2, Zusatzanalysen

4.2.6 Sicherheit

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Safety Population
TEAE
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	108 (91.5)	240 (98.4)
Number of Subjects Censored, n (%)	10 (8.5)	4 (1.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.13 (0.07, 0.23)	0.10 (0.07, 0.13)
Median (95% CI)	0.46 (0.36, 0.66)	0.30 (0.23, 0.46)
75% percentile (95% CI)	0.72 (0.69, 1.02)	0.69 (NE, NE)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.369 (0.120)
95% CI		(1.082, 1.731)
Log-rank p-value		0.009

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
TEAE
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	8.5 (3.4, 13.5)	2.0 (0.3, 3.8)
6 months	NE (NE, NE)	1.4 (0.0, 3.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
TEAE
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	105 (93.8)	211 (99.5)
Number of Subjects Censored, n (%)	7 (6.3)	1 (0.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.20)	0.07 (NE, NE)
Median (95% CI)	0.46 (0.30, 0.62)	0.23 (0.16, 0.30)
75% percentile (95% CI)	0.69 (0.69, 0.92)	0.69 (0.46, 0.69)
Min, Max	0.0, 3.6	0.0, 3.7
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.451 (0.123)
95% CI		(1.140, 1.845)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
TEAE
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	6.9 (2.2, 11.7)	1.4 (0.0, 3.0)
6 months	0.0 (NE, NE)	0.0 (NE, NE)
9 months	0.0 (NE, NE)	0.0 (NE, NE)
12 months	0.0 (NE, NE)	0.0 (NE, NE)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.46	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
Serious TEAE
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	41 (34.7)	93 (38.1)
Number of Subjects Censored, n (%)	77 (65.3)	151 (61.9)
Time to first TEAE (months)		
25% percentile (95% CI)	1.31 (0.95, 2.33)	2.86 (1.87, 3.58)
Median (95% CI)	NE (4.14, NE)	7.82 (6.90, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (11.04, NE)
Min, Max	0.1, 6.8*	0.1, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.769 (0.194)
95% CI		(0.525, 1.125)
Log-rank p-value		0.254

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
Serious TEAE
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	66.5 (57.9, 75.1)	73.3 (67.7, 79.0)
6 months	60.7 (49.5, 71.8)	58.1 (50.8, 65.4)
9 months	NE (NE, NE)	47.9 (38.3, 57.5)
12 months	NE (NE, NE)	39.9 (23.6, 56.3)
18 months	NE (NE, NE)	39.9 (23.6, 56.3)
Median Follow-up Time (months)	2.83	3.19

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
Serious TEAE
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	47 (42.0)	78 (36.8)
Number of Subjects Censored, n (%)	65 (58.0)	134 (63.2)
Time to first TEAE (months)		
25% percentile (95% CI)	1.28 (0.79, 2.04)	2.43 (1.77, 3.29)
Median (95% CI)	3.65 (2.40, NE)	11.96 (7.79, NE)
75% percentile (95% CI)	NE (5.36, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.623 (0.191)
95% CI		(0.428, 0.906)
Log-rank p-value		0.015

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
Serious TEAE
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	60.0 (50.6, 69.4)	70.8 (64.5, 77.0)
6 months	39.9 (19.5, 60.4)	59.9 (52.1, 67.7)
9 months	39.9 (19.5, 60.4)	53.8 (44.0, 63.6)
12 months	39.9 (19.5, 60.4)	44.5 (29.4, 59.5)
18 months	NE (NE, NE)	44.5 (29.4, 59.5)
Median Follow-up Time (months)	2.43	3.48

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
TEAE ≤ CTCAE Grade 2
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	104 (88.1)	238 (97.5)
Number of Subjects Censored, n (%)	14 (11.9)	6 (2.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.13 (0.07, 0.26)	0.10 (0.07, 0.13)
Median (95% CI)	0.53 (0.36, 0.69)	0.36 (0.26, 0.49)
75% percentile (95% CI)	0.82 (0.69, 1.38)	0.69 (NE, NE)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.386 (0.121)
95% CI		(1.093, 1.758)
Log-rank p-value		0.007

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
TEAE ≤ CTCAE Grade 2
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	10.8 (5.0, 16.6)	2.3 (0.4, 4.3)
6 months	NE (NE, NE)	1.6 (0.0, 3.4)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.53	0.36

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
TEAE ≤ CTCAE Grade 2
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	96 (85.7)	206 (97.2)
Number of Subjects Censored, n (%)	16 (14.3)	6 (2.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.56 (0.33, 0.69)	0.26 (0.20, 0.36)
75% percentile (95% CI)	0.72 (0.69, 1.61)	0.69 (0.62, 0.69)
Min, Max	0.0, 4.7*	0.0, 3.7
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.519 (0.126)
95% CI		(1.186, 1.946)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
TEAE ≤ CTCAE Grade 2
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	12.3 (5.8, 18.7)	2.4 (0.1, 4.8)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.56	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
TEAE ≥ CTCAE Grade 3
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	53 (44.9)	153 (62.7)
Number of Subjects Censored, n (%)	65 (55.1)	91 (37.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.99 (0.72, 1.38)	0.95 (0.69, 1.28)
Median (95% CI)	4.14 (2.27, NE)	2.86 (2.00, 3.71)
75% percentile (95% CI)	NE (NE, NE)	11.04 (6.90, NE)
Min, Max	0.1, 6.8*	0.0, 16.1
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.278 (0.163)
95% CI		(0.928, 1.759)
Log-rank p-value		0.085

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
TEAE ≥ CTCAE Grade 3
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	58.1 (49.2, 67.1)	49.0 (42.7, 55.4)
6 months	46.5 (33.9, 59.1)	34.2 (27.3, 41.1)
9 months	NE (NE, NE)	26.2 (18.4, 34.1)
12 months	NE (NE, NE)	21.0 (9.9, 32.1)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.51	2.74

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
TEAE ≥ CTCAE Grade 3
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	63 (56.3)	133 (62.7)
Number of Subjects Censored, n (%)	49 (43.8)	79 (37.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.69, 1.25)	0.95 (0.69, 1.35)
Median (95% CI)	2.40 (1.87, 4.83)	2.79 (1.97, 3.98)
75% percentile (95% CI)	5.36 (4.83, NE)	8.90 (6.67, NE)
Min, Max	0.1, 9.3	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.950 (0.158)
95% CI		(0.697, 1.293)
Log-rank p-value		0.729

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
TEAE ≥ CTCAE Grade 3
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	49.9 (40.5, 59.3)	47.6 (40.8, 54.5)
6 months	15.8 (0.0, 33.2)	34.0 (26.5, 41.6)
9 months	15.8 (0.0, 33.2)	23.6 (14.2, 32.9)
12 months	0.0 (NE, NE)	15.9 (4.4, 27.4)
18 months	0.0 (NE, NE)	15.9 (4.4, 27.4)
Median Follow-up Time (months)	2.00	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
Discontinuation due to TEAE
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	24 (20.3)	44 (18.0)
Number of Subjects Censored, n (%)	94 (79.7)	200 (82.0)
Time to first TEAE (months)		
25% percentile (95% CI)	4.57 (1.81, NE)	8.21 (5.32, 11.04)
Median (95% CI)	NE (NE, NE)	NE (11.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.541 (0.269)
95% CI		(0.320, 0.916)
Log-rank p-value		0.029

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
Discontinuation due to TEAE
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.9 (74.8, 88.9)	89.2 (85.3, 93.1)
6 months	71.0 (57.7, 84.2)	81.6 (75.7, 87.4)
9 months	NE (NE, NE)	71.4 (62.1, 80.7)
12 months	NE (NE, NE)	58.8 (40.2, 77.4)
18 months	NE (NE, NE)	58.8 (40.2, 77.4)
Median Follow-up Time (months)	2.83	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
Discontinuation due to TEAE
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	25 (22.3)	49 (23.1)
Number of Subjects Censored, n (%)	87 (77.7)	163 (76.9)
Time to first TEAE (months)		
25% percentile (95% CI)	3.65 (1.71, NE)	6.18 (4.11, 8.38)
Median (95% CI)	NE (3.98, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.693 (0.257)
95% CI		(0.418, 1.147)
Log-rank p-value		0.196

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
Discontinuation due to TEAE
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.7 (73.2, 88.1)	83.4 (78.3, 88.5)
6 months	57.9 (35.9, 79.8)	75.2 (68.2, 82.2)
9 months	57.9 (35.9, 79.8)	63.3 (52.5, 74.1)
12 months	57.9 (35.9, 79.8)	63.3 (52.5, 74.1)
18 months	NE (NE, NE)	63.3 (52.5, 74.1)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
Deaths (Grade 5 TEAEs)
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	20 (16.9)	26 (10.7)
Number of Subjects Censored, n (%)	98 (83.1)	218 (89.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.76, NE)	12.22 (9.69, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.392 (0.315)
95% CI		(0.212, 0.727)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
Deaths (Grade 5 TEAEs)
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.8 (75.6, 89.9)	94.5 (91.6, 97.4)
6 months	80.3 (71.8, 88.7)	88.0 (83.0, 92.9)
9 months	NE (NE, NE)	84.5 (77.7, 91.4)
12 months	NE (NE, NE)	79.5 (68.1, 91.0)
18 months	NE (NE, NE)	63.6 (34.3, 93.0)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
Deaths (Grade 5 TEAEs)
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	25 (22.3)	22 (10.4)
Number of Subjects Censored, n (%)	87 (77.7)	190 (89.6)
Time to first TEAE (months)		
25% percentile (95% CI)	3.75 (2.20, NE)	NE (8.87, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.314 (0.311)
95% CI		(0.171, 0.577)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3B
Summary of Time to Onset of Overall TEAE by Age
Safety Population
Deaths (Grade 5 TEAEs)
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.7 (69.5, 85.8)	93.0 (89.5, 96.6)
6 months	68.5 (54.4, 82.5)	86.4 (80.3, 92.6)
9 months	68.5 (54.4, 82.5)	81.8 (73.0, 90.7)
12 months	68.5 (54.4, 82.5)	81.8 (73.0, 90.7)
18 months	NE (NE, NE)	81.8 (73.0, 90.7)
Median Follow-up Time (months)	2.79	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
TEAE
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	127 (90.7)	238 (98.8)
Number of Subjects Censored, n (%)	13 (9.3)	3 (1.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.30, 0.62)	0.26 (0.20, 0.36)
75% percentile (95% CI)	0.72 (0.69, 1.25)	0.69 (0.62, 0.69)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.417 (0.113)
95% CI		(1.136, 1.769)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
TEAE
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	9.1 (4.3, 13.9)	1.7 (0.0, 3.3)
6 months	NE (NE, NE)	1.1 (0.0, 2.5)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
TEAE
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	86 (95.6)	213 (99.1)
Number of Subjects Censored, n (%)	4 (4.4)	2 (0.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.16 (0.07, 0.26)	0.07 (0.07, 0.10)
Median (95% CI)	0.51 (0.33, 0.66)	0.26 (0.20, 0.36)
75% percentile (95% CI)	0.69 (0.69, 0.92)	0.69 (0.59, 0.69)
Min, Max	0.0, 3.6	0.0, 5.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.342 (0.131)
95% CI		(1.039, 1.733)
Log-rank p-value		0.030

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
TEAE
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	5.6 (0.8, 10.3)	1.9 (0.1, 3.7)
6 months	0.0 (NE, NE)	0.0 (NE, NE)
9 months	0.0 (NE, NE)	0.0 (NE, NE)
12 months	0.0 (NE, NE)	0.0 (NE, NE)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.51	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
Serious TEAE
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	57 (40.7)	93 (38.6)
Number of Subjects Censored, n (%)	83 (59.3)	148 (61.4)
Time to first TEAE (months)		
25% percentile (95% CI)	1.18 (0.76, 1.81)	2.53 (1.61, 3.25)
Median (95% CI)	4.14 (3.15, NE)	8.28 (6.90, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.604 (0.176)
95% CI		(0.428, 0.854)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
Serious TEAE
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	61.2 (53.0, 69.4)	71.0 (65.1, 76.8)
6 months	48.4 (34.5, 62.3)	59.3 (52.3, 66.3)
9 months	48.4 (34.5, 62.3)	49.1 (39.1, 59.2)
12 months	48.4 (34.5, 62.3)	45.9 (34.6, 57.1)
18 months	NE (NE, NE)	45.9 (34.6, 57.1)
Median Follow-up Time (months)	2.58	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
Serious TEAE
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	31 (34.4)	78 (36.3)
Number of Subjects Censored, n (%)	59 (65.6)	137 (63.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.68 (1.02, 3.65)	2.76 (1.87, 4.07)
Median (95% CI)	NE (5.36, NE)	11.04 (6.01, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (11.96, NE)
Min, Max	0.2, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.762 (0.218)
95% CI		(0.497, 1.169)
Log-rank p-value		0.252

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
Serious TEAE
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	66.7 (56.8, 76.7)	73.7 (67.6, 79.7)
6 months	57.9 (43.1, 72.7)	59.0 (51.0, 67.0)
9 months	NE (NE, NE)	51.9 (42.0, 61.8)
12 months	NE (NE, NE)	33.3 (11.0, 55.7)
18 months	NE (NE, NE)	33.3 (11.0, 55.7)
Median Follow-up Time (months)	2.83	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
TEAE ≤ CTCAE Grade 2
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	119 (85.0)	233 (96.7)
Number of Subjects Censored, n (%)	21 (15.0)	8 (3.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.48 (0.36, 0.69)	0.26 (0.23, 0.39)
75% percentile (95% CI)	0.82 (0.69, 1.61)	0.69 (NE, NE)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.446 (0.116)
95% CI		(1.153, 1.814)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
TEAE ≤ CTCAE Grade 2
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	13.3 (7.4, 19.3)	2.7 (0.5, 4.9)
6 months	NE (NE, NE)	1.8 (0.0, 3.8)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.48	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
TEAE ≤ CTCAE Grade 2
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	81 (90.0)	211 (98.1)
Number of Subjects Censored, n (%)	9 (10.0)	4 (1.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.16 (0.07, 0.26)	0.10 (0.07, 0.13)
Median (95% CI)	0.59 (0.36, 0.69)	0.33 (0.23, 0.46)
75% percentile (95% CI)	0.72 (0.69, 1.02)	0.69 (NE, NE)
Min, Max	0.0, 4.7*	0.0, 5.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.384 (0.133)
95% CI		(1.066, 1.797)
Log-rank p-value		0.025

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
TEAE ≤ CTCAE Grade 2
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	8.3 (2.3, 14.3)	2.3 (0.2, 4.3)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.59	0.33

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
TEAE ≥ CTCAE Grade 3
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	68 (48.6)	146 (60.6)
Number of Subjects Censored, n (%)	72 (51.4)	95 (39.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.94 (0.69, 1.28)	1.15 (0.69, 1.35)
Median (95% CI)	3.35 (2.27, NE)	3.19 (2.53, 3.71)
75% percentile (95% CI)	9.26 (4.14, NE)	9.20 (7.33, NE)
Min, Max	0.1, 9.3	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.014 (0.151)
95% CI		(0.755, 1.363)
Log-rank p-value		0.879

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
TEAE ≥ CTCAE Grade 3
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	55.7 (47.3, 64.0)	50.6 (44.2, 57.1)
6 months	38.2 (24.4, 52.0)	37.2 (30.3, 44.0)
9 months	38.2 (24.4, 52.0)	27.9 (18.9, 36.9)
12 months	0.0 (NE, NE)	23.9 (13.4, 34.5)
18 months	0.0 (NE, NE)	12.0 (0.0, 29.4)
Median Follow-up Time (months)	2.30	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
TEAE ≥ CTCAE Grade 3
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	48 (53.3)	140 (65.1)
Number of Subjects Censored, n (%)	42 (46.7)	75 (34.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.69, 1.38)	0.72 (0.62, 0.95)
Median (95% CI)	3.65 (1.87, 5.55)	2.56 (1.84, 3.84)
75% percentile (95% CI)	NE (5.36, NE)	8.38 (5.98, NE)
Min, Max	0.2, 6.8*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.164 (0.171)
95% CI		(0.833, 1.627)
Log-rank p-value		0.306

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
TEAE ≥ CTCAE Grade 3
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	51.8 (41.4, 62.2)	45.9 (39.2, 52.6)
6 months	31.8 (16.3, 47.3)	31.3 (23.9, 38.8)
9 months	NE (NE, NE)	22.0 (13.6, 30.4)
12 months	NE (NE, NE)	12.2 (0.5, 23.9)
18 months	NE (NE, NE)	12.2 (0.5, 23.9)
Median Follow-up Time (months)	2.25	2.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
Discontinuation due to TEAE
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	29 (20.7)	45 (18.7)
Number of Subjects Censored, n (%)	111 (79.3)	196 (81.3)
Time to first TEAE (months)		
25% percentile (95% CI)	3.98 (1.81, NE)	8.21 (5.39, NE)
Median (95% CI)	NE (4.57, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.3, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.592 (0.251)
95% CI		(0.362, 0.970)
Log-rank p-value		0.032

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
Discontinuation due to TEAE
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.6 (75.0, 88.1)	86.9 (82.6, 91.2)
6 months	65.9 (50.1, 81.7)	80.2 (74.4, 86.1)
9 months	65.9 (50.1, 81.7)	70.7 (61.2, 80.3)
12 months	65.9 (50.1, 81.7)	70.7 (61.2, 80.3)
18 months	NE (NE, NE)	70.7 (61.2, 80.3)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
Discontinuation due to TEAE
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	20 (22.2)	48 (22.3)
Number of Subjects Censored, n (%)	70 (77.8)	167 (77.7)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (1.71, NE)	6.60 (4.76, 8.90)
Median (95% CI)	NE (4.83, NE)	NE (9.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.615 (0.281)
95% CI		(0.355, 1.066)
Log-rank p-value		0.128

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
Discontinuation due to TEAE
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.8 (72.5, 89.0)	86.1 (81.4, 90.8)
6 months	64.4 (45.9, 82.9)	77.1 (70.3, 83.9)
9 months	NE (NE, NE)	64.6 (54.0, 75.2)
12 months	NE (NE, NE)	55.3 (40.1, 70.5)
18 months	NE (NE, NE)	55.3 (40.1, 70.5)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
Deaths (Grade 5 TEAEs)
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	30 (21.4)	24 (10.0)
Number of Subjects Censored, n (%)	110 (78.6)	217 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	3.75 (2.33, NE)	NE (8.87, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.7, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.296 (0.289)
95% CI		(0.168, 0.522)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
Deaths (Grade 5 TEAEs)
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.7 (72.8, 86.6)	94.0 (91.0, 97.1)
6 months	68.9 (55.8, 82.1)	87.1 (81.8, 92.4)
9 months	68.9 (55.8, 82.1)	83.8 (75.6, 92.0)
12 months	68.9 (55.8, 82.1)	83.8 (75.6, 92.0)
18 months	NE (NE, NE)	83.8 (75.6, 92.0)
Median Follow-up Time (months)	2.83	4.11

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
Deaths (Grade 5 TEAEs)
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	15 (16.7)	24 (11.2)
Number of Subjects Censored, n (%)	75 (83.3)	191 (88.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.30, NE)	12.22 (8.21, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 8.4*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.419 (0.348)
95% CI		(0.212, 0.828)
Log-rank p-value		0.012

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
TEAE
North America

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.1 (72.4, 89.8)	93.6 (90.3, 97.0)
6 months	81.1 (72.4, 89.8)	87.8 (82.2, 93.4)
9 months	NE (NE, NE)	83.1 (75.5, 90.6)
12 months	NE (NE, NE)	78.4 (67.1, 89.8)
18 months	NE (NE, NE)	65.4 (40.1, 90.6)
Median Follow-up Time (months)	2.83	3.78

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	39 (95.1)	79 (98.8)
Number of Subjects Censored, n (%)	2 (4.9)	1 (1.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.20 (0.03, 0.43)	0.13 (0.07, 0.16)
Median (95% CI)	0.49 (0.33, 0.69)	0.36 (0.23, 0.46)
75% percentile (95% CI)	0.72 (0.69, 1.02)	0.69 (0.46, 0.69)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
TEAE
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Min, Max	0.0, 4.6*	0.0, 3.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.519 (0.203)
95% CI		(1.021, 2.259)
Log-rank p-value		0.043

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
TEAE
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	4.9 (0.0, 11.5)	1.2 (0.0, 3.7)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.49	0.36

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
TEAE
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	155 (92.8)	324 (99.1)
Number of Subjects Censored, n (%)	12 (7.2)	3 (0.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.10)	0.07 (NE, NE)
Median (95% CI)	0.46 (0.30, 0.59)	0.23 (0.20, 0.33)
75% percentile (95% CI)	0.69 (0.69, 0.82)	0.69 (NE, NE)
Min, Max	0.0, 3.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.310 (0.099)
95% CI		(1.078, 1.592)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
TEAE
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	7.7 (3.6, 11.7)	1.8 (0.4, 3.3)
6 months	NE (NE, NE)	0.7 (0.0, 1.7)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
TEAE
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	19 (86.4)	48 (98.0)
Number of Subjects Censored, n (%)	3 (13.6)	1 (2.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.33 (0.13, 0.39)	0.10 (0.07, 0.20)
Median (95% CI)	0.43 (0.33, 0.95)	0.26 (0.16, 0.30)
75% percentile (95% CI)	1.61 (0.46, NE)	0.46 (0.30, 0.69)
Min, Max	0.1, 2.8*	0.0, 3.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.252 (0.310)
95% CI		(1.227, 4.133)
Log-rank p-value		0.008

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
TEAE
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	NE (NE, NE)	2.0 (0.0, 6.0)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.43	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
Serious TEAE
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	15 (36.6)	36 (45.0)
Number of Subjects Censored, n (%)	26 (63.4)	44 (55.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.94 (0.89, 4.14)	1.61 (0.82, 3.25)
Median (95% CI)	NE (2.04, NE)	4.80 (3.29, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (7.79, NE)
Min, Max	0.3, 8.4*	0.1, 12.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.966 (0.321)
95% CI		(0.515, 1.811)
Log-rank p-value		0.784

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
Serious TEAE
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	63.1 (47.4, 78.8)	65.4 (54.5, 76.4)
6 months	52.6 (29.7, 75.5)	43.1 (28.9, 57.3)
9 months	NE (NE, NE)	35.9 (18.4, 53.4)
12 months	NE (NE, NE)	35.9 (18.4, 53.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.37	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
Serious TEAE
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	68 (40.7)	118 (36.1)
Number of Subjects Censored, n (%)	99 (59.3)	209 (63.9)
Time to first TEAE (months)		
25% percentile (95% CI)	1.15 (0.76, 1.54)	2.76 (2.04, 3.58)
Median (95% CI)	NE (3.35, NE)	11.04 (7.82, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.600 (0.158)
95% CI		(0.440, 0.817)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
Serious TEAE
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	61.8 (54.3, 69.2)	73.1 (68.2, 78.0)
6 months	50.7 (38.7, 62.7)	62.5 (56.5, 68.5)
9 months	50.7 (38.7, 62.7)	53.3 (45.0, 61.5)
12 months	50.7 (38.7, 62.7)	42.7 (29.5, 55.8)
18 months	NE (NE, NE)	42.7 (29.5, 55.8)
Median Follow-up Time (months)	2.79	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
Serious TEAE
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	5 (22.7)	17 (34.7)
Number of Subjects Censored, n (%)	17 (77.3)	32 (65.3)
Time to first TEAE (months)		
25% percentile (95% CI)	2.37 (0.23, NE)	3.02 (0.95, 5.95)
Median (95% CI)	NE (2.37, NE)	NE (4.90, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.5*	0.5, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.728 (0.557)
95% CI		(0.244, 2.168)
Log-rank p-value		0.474

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
Serious TEAE
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	74.0 (54.0, 94.1)	77.1 (65.2, 89.0)
6 months	74.0 (54.0, 94.1)	59.6 (42.7, 76.5)
9 months	NE (NE, NE)	55.0 (37.2, 72.9)
12 months	NE (NE, NE)	55.0 (37.2, 72.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
TEAE ≤ CTCAE Grade 2
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	36 (87.8)	79 (98.8)
Number of Subjects Censored, n (%)	5 (12.2)	1 (1.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.20 (0.03, 0.46)	0.15 (0.10, 0.23)
Median (95% CI)	0.62 (0.39, 0.69)	0.39 (0.26, 0.46)
75% percentile (95% CI)	0.72 (0.69, 1.61)	0.69 (0.56, 0.69)
Min, Max	0.0, 4.6*	0.0, 3.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.576 (0.207)
95% CI		(1.051, 2.365)
Log-rank p-value		0.035

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
TEAE ≤ CTCAE Grade 2
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	11.4 (1.4, 21.4)	1.2 (0.0, 3.7)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.62	0.39

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
TEAE ≤ CTCAE Grade 2
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	146 (87.4)	318 (97.2)
Number of Subjects Censored, n (%)	21 (12.6)	9 (2.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.10)	0.07 (NE, NE)
Median (95% CI)	0.56 (0.30, 0.69)	0.26 (0.23, 0.39)
75% percentile (95% CI)	0.76 (0.69, 1.25)	0.69 (NE, NE)
Min, Max	0.0, 4.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.358 (0.101)
95% CI		(1.113, 1.657)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
TEAE ≤ CTCAE Grade 2
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	10.5 (5.6, 15.5)	2.7 (0.8, 4.6)
6 months	NE (NE, NE)	1.1 (0.0, 2.5)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.56	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
TEAE ≤ CTCAE Grade 2
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	18 (81.8)	47 (95.9)
Number of Subjects Censored, n (%)	4 (18.2)	2 (4.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.33 (0.13, 0.39)	0.13 (0.07, 0.23)
Median (95% CI)	0.43 (0.33, 0.95)	0.26 (0.23, 0.36)
75% percentile (95% CI)	1.61 (0.46, NE)	0.66 (0.36, 0.69)
Min, Max	0.1, 2.8*	0.0, 3.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.997 (0.313)
95% CI		(1.081, 3.689)
Log-rank p-value		0.040

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
TEAE ≤ CTCAE Grade 2
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	NE (NE, NE)	2.6 (0.0, 7.4)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.43	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	19 (46.3)	54 (67.5)
Number of Subjects Censored, n (%)	22 (53.7)	26 (32.5)
Time to first TEAE (months)		
25% percentile (95% CI)	1.35 (0.62, 2.00)	0.71 (0.53, 1.28)
Median (95% CI)	4.14 (1.94, NE)	1.87 (1.41, 3.35)
75% percentile (95% CI)	5.55 (NE, NE)	5.26 (3.61, NE)
Min, Max	0.3, 5.6	0.1, 12.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.444 (0.273)
95% CI		(0.846, 2.465)
Log-rank p-value		0.127

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	56.9 (41.3, 72.5)	41.7 (30.5, 52.9)
6 months	0.0 (NE, NE)	24.6 (13.1, 36.2)
9 months	0.0 (NE, NE)	18.5 (4.9, 32.0)
12 months	0.0 (NE, NE)	18.5 (4.9, 32.0)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.04	1.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	89 (53.3)	199 (60.9)
Number of Subjects Censored, n (%)	78 (46.7)	128 (39.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.92 (0.72, 1.15)	1.12 (0.72, 1.31)
Median (95% CI)	3.19 (1.87, 4.83)	3.19 (2.53, 4.47)
75% percentile (95% CI)	9.26 (5.36, NE)	9.20 (7.39, NE)
Min, Max	0.1, 9.3	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.938 (0.131)
95% CI		(0.727, 1.212)
Log-rank p-value		0.739

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	51.9 (44.2, 59.5)	50.5 (45.0, 56.0)
6 months	34.0 (21.3, 46.7)	37.9 (31.8, 43.9)
9 months	34.0 (21.3, 46.7)	26.7 (19.2, 34.1)
12 months	0.0 (NE, NE)	17.6 (7.3, 27.9)
18 months	0.0 (NE, NE)	11.7 (0.1, 23.4)
Median Follow-up Time (months)	2.27	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	8 (36.4)	33 (67.3)
Number of Subjects Censored, n (%)	14 (63.6)	16 (32.7)
Time to first TEAE (months)		
25% percentile (95% CI)	2.27 (0.23, 4.34)	0.69 (0.46, 1.54)
Median (95% CI)	4.34 (2.27, NE)	2.56 (1.18, 3.71)
75% percentile (95% CI)	NE (4.34, NE)	4.90 (3.25, NE)
Min, Max	0.2, 6.5*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.521 (0.410)
95% CI		(0.681, 3.398)
Log-rank p-value		0.390

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	64.4 (42.5, 86.3)	44.9 (31.0, 58.8)
6 months	32.2 (0.0, 78.1)	23.5 (8.1, 38.9)
9 months	NE (NE, NE)	23.5 (8.1, 38.9)
12 months	NE (NE, NE)	23.5 (8.1, 38.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.32	2.56

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
Discontinuation due to TEAE
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	8 (19.5)	14 (17.5)
Number of Subjects Censored, n (%)	33 (80.5)	66 (82.5)
Time to first TEAE (months)		
25% percentile (95% CI)	4.57 (1.35, NE)	8.21 (4.11, NE)
Median (95% CI)	NE (4.57, NE)	NE (8.21, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 8.4*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.504 (0.467)
95% CI		(0.202, 1.258)
Log-rank p-value		0.205

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
Discontinuation due to TEAE
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.0 (69.9, 94.1)	91.0 (84.5, 97.4)
6 months	68.4 (41.9, 94.8)	82.7 (71.9, 93.5)
9 months	NE (NE, NE)	57.4 (34.7, 80.1)
12 months	NE (NE, NE)	57.4 (34.7, 80.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
Discontinuation due to TEAE
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	38 (22.8)	71 (21.7)
Number of Subjects Censored, n (%)	129 (77.2)	256 (78.3)
Time to first TEAE (months)		
25% percentile (95% CI)	3.65 (1.71, NE)	7.03 (4.76, 11.04)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.660 (0.209)
95% CI		(0.439, 0.994)
Log-rank p-value		0.047

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
Discontinuation due to TEAE
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.9 (73.7, 86.0)	84.4 (80.4, 88.4)
6 months	66.1 (53.0, 79.3)	77.1 (71.7, 82.4)
9 months	66.1 (53.0, 79.3)	69.7 (62.2, 77.3)
12 months	66.1 (53.0, 79.3)	64.1 (53.7, 74.4)
18 months	NE (NE, NE)	64.1 (53.7, 74.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
Discontinuation due to TEAE
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	3 (13.6)	8 (16.3)
Number of Subjects Censored, n (%)	19 (86.4)	41 (83.7)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (0.23, NE)	8.28 (4.27, NE)
Median (95% CI)	4.34 (4.34, NE)	NE (8.28, NE)
75% percentile (95% CI)	NE (4.34, NE)	NE (NE, NE)
Min, Max	0.2, 6.5*	0.5, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.177 (0.889)
95% CI		(0.031, 1.009)
Log-rank p-value		0.028

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
Discontinuation due to TEAE
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (78.9, 100.0)	93.8 (87.1, 100.0)
6 months	45.5 (0.0, 100.0)	82.3 (68.5, 96.2)
9 months	NE (NE, NE)	62.9 (35.8, 90.0)
12 months	NE (NE, NE)	62.9 (35.8, 90.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
Deaths (Grade 5 TEAEs)
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	5 (12.2)	9 (11.3)
Number of Subjects Censored, n (%)	36 (87.8)	71 (88.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.94, NE)	NE (4.60, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 8.4*	0.8, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.448 (0.594)
95% CI		(0.140, 1.434)
Log-rank p-value		0.257

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
Deaths (Grade 5 TEAEs)
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.1 (76.4, 97.7)	96.0 (91.5, 100.0)
6 months	87.1 (76.4, 97.7)	86.8 (77.3, 96.3)
9 months	NE (NE, NE)	75.5 (57.9, 93.1)
12 months	NE (NE, NE)	75.5 (57.9, 93.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
Deaths (Grade 5 TEAEs)
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	37 (22.2)	34 (10.4)
Number of Subjects Censored, n (%)	130 (77.8)	293 (89.6)
Time to first TEAE (months)		
25% percentile (95% CI)	3.75 (2.33, NE)	NE (9.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.306 (0.249)
95% CI		(0.187, 0.498)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
Deaths (Grade 5 TEAEs)
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.4 (71.9, 84.9)	93.0 (90.2, 95.8)
6 months	71.2 (61.3, 81.2)	88.1 (83.8, 92.4)
9 months	71.2 (61.3, 81.2)	85.0 (78.8, 91.2)
12 months	71.2 (61.3, 81.2)	82.2 (74.2, 90.3)
18 months	NE (NE, NE)	75.9 (61.9, 89.9)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3D
Summary of Time to Onset of Overall TEAE by Geographic Region
Safety Population
Deaths (Grade 5 TEAEs)
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	3 (13.6)	5 (10.2)
Number of Subjects Censored, n (%)	19 (86.4)	44 (89.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.68, NE)	NE (4.27, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.258 (0.845)
95% CI		(0.049, 1.352)
Log-rank p-value		0.055

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
TEAE
ECOG: 0

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.6 (62.5, 100.0)	95.9 (90.4, 100.0)
6 months	81.6 (62.5, 100.0)	84.2 (70.6, 97.9)
9 months	NE (NE, NE)	84.2 (70.6, 97.9)
12 months	NE (NE, NE)	84.2 (70.6, 97.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	91 (89.2)	189 (97.9)
Number of Subjects Censored, n (%)	11 (10.8)	4 (2.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.13 (0.07, 0.30)	0.10 (0.07, 0.13)
Median (95% CI)	0.59 (0.46, 0.69)	0.26 (0.23, 0.36)
75% percentile (95% CI)	0.95 (0.69, 1.87)	0.69 (0.59, 0.69)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
TEAE
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Min, Max	0.0, 3.6	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.720 (0.133)
95% CI		(1.325, 2.233)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
TEAE
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	11.5 (5.2, 17.8)	2.1 (0.1, 4.1)
6 months	0.0 (NE, NE)	2.1 (0.1, 4.1)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.59	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
TEAE
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	122 (95.3)	262 (99.6)
Number of Subjects Censored, n (%)	6 (4.7)	1 (0.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.20)	0.07 (NE, NE)
Median (95% CI)	0.39 (0.26, 0.53)	0.26 (0.20, 0.36)
75% percentile (95% CI)	0.69 (0.69, 0.76)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.6*	0.0, 5.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.222 (0.112)
95% CI		(0.981, 1.523)
Log-rank p-value		0.039

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
TEAE
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	4.7 (1.0, 8.3)	1.5 (0.0, 3.0)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.39	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
Serious TEAE
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	31 (30.4)	65 (33.7)
Number of Subjects Censored, n (%)	71 (69.6)	128 (66.3)
Time to first TEAE (months)		
25% percentile (95% CI)	2.33 (1.31, 4.14)	4.17 (2.96, 5.72)
Median (95% CI)	NE (4.14, NE)	9.23 (7.79, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (11.96, NE)
Min, Max	0.1, 8.4*	0.1, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.669 (0.231)
95% CI		(0.425, 1.053)
Log-rank p-value		0.144

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
Serious TEAE
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.0 (64.3, 81.8)	80.3 (74.6, 86.0)
6 months	60.2 (46.4, 74.0)	66.7 (59.0, 74.5)
9 months	NE (NE, NE)	53.2 (42.6, 63.7)
12 months	NE (NE, NE)	41.3 (23.5, 59.1)
18 months	NE (NE, NE)	41.3 (23.5, 59.1)
Median Follow-up Time (months)	2.83	4.44

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
Serious TEAE
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	57 (44.5)	106 (40.3)
Number of Subjects Censored, n (%)	71 (55.5)	157 (59.7)
Time to first TEAE (months)		
25% percentile (95% CI)	0.99 (0.72, 1.31)	1.87 (1.58, 2.56)
Median (95% CI)	5.36 (2.23, NE)	11.04 (4.50, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.661 (0.168)
95% CI		(0.475, 0.919)
Log-rank p-value		0.015

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
Serious TEAE
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	55.5 (46.6, 64.4)	66.1 (60.3, 72.0)
6 months	46.7 (31.9, 61.4)	52.8 (45.5, 60.1)
9 months	46.7 (31.9, 61.4)	50.2 (41.6, 58.8)
12 months	46.7 (31.9, 61.4)	44.6 (31.8, 57.4)
18 months	NE (NE, NE)	44.6 (31.8, 57.4)
Median Follow-up Time (months)	2.02	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
TEAE ≤ CTCAE Grade 2
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	86 (84.3)	188 (97.4)
Number of Subjects Censored, n (%)	16 (15.7)	5 (2.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.13 (0.07, 0.30)	0.10 (0.07, 0.13)
Median (95% CI)	0.66 (0.46, 0.69)	0.30 (0.23, 0.39)
75% percentile (95% CI)	1.02 (0.69, 1.87)	0.69 (NE, NE)
Min, Max	0.0, 4.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.699 (0.136)
95% CI		(1.303, 2.217)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
TEAE ≤ CTCAE Grade 2
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	14.5 (7.5, 21.6)	2.3 (0.1, 4.5)
6 months	NE (NE, NE)	2.3 (0.1, 4.5)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.66	0.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
TEAE ≤ CTCAE Grade 2
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	114 (89.1)	256 (97.3)
Number of Subjects Censored, n (%)	14 (10.9)	7 (2.7)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.30, 0.62)	0.30 (0.23, 0.46)
75% percentile (95% CI)	0.72 (0.69, 1.02)	0.69 (NE, NE)
Min, Max	0.0, 4.6*	0.0, 5.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.288 (0.115)
95% CI		(1.028, 1.614)
Log-rank p-value		0.015

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
TEAE ≤ CTCAE Grade 2
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	8.6 (3.2, 13.9)	2.7 (0.6, 4.8)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.46	0.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
TEAE ≥ CTCAE Grade 3
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	37 (36.3)	119 (61.7)
Number of Subjects Censored, n (%)	65 (63.7)	74 (38.3)
Time to first TEAE (months)		
25% percentile (95% CI)	2.00 (0.95, 3.35)	1.18 (0.69, 1.51)
Median (95% CI)	4.83 (3.65, NE)	3.65 (2.69, 5.19)
75% percentile (95% CI)	NE (5.55, NE)	9.20 (7.10, NE)
Min, Max	0.1, 6.5*	0.0, 16.1
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.474 (0.194)
95% CI		(1.008, 2.154)
Log-rank p-value		0.036

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
TEAE ≥ CTCAE Grade 3
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	70.2 (61.3, 79.2)	54.4 (47.3, 61.5)
6 months	37.0 (15.3, 58.6)	38.0 (30.2, 45.8)
9 months	NE (NE, NE)	25.2 (16.3, 34.1)
12 months	NE (NE, NE)	14.4 (1.1, 27.7)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
TEAE ≥ CTCAE Grade 3
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	79 (61.7)	167 (63.5)
Number of Subjects Censored, n (%)	49 (38.3)	96 (36.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.72 (0.69, 0.95)	0.85 (0.69, 1.15)
Median (95% CI)	1.87 (1.28, 2.40)	2.53 (1.84, 2.86)
75% percentile (95% CI)	9.26 (3.71, NE)	11.04 (6.05, NE)
Min, Max	0.1, 9.3	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.863 (0.139)
95% CI		(0.657, 1.133)
Log-rank p-value		0.371

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
TEAE ≥ CTCAE Grade 3
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	41.2 (32.5, 49.9)	44.0 (37.9, 50.1)
6 months	28.5 (15.2, 41.8)	31.6 (24.9, 38.3)
9 months	28.5 (15.2, 41.8)	25.7 (17.2, 34.1)
12 months	0.0 (NE, NE)	22.0 (12.2, 31.8)
18 months	0.0 (NE, NE)	22.0 (12.2, 31.8)
Median Follow-up Time (months)	1.87	2.00

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
Discontinuation due to TEAE
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	17 (16.7)	32 (16.6)
Number of Subjects Censored, n (%)	85 (83.3)	161 (83.4)
Time to first TEAE (months)		
25% percentile (95% CI)	4.57 (3.19, NE)	7.52 (6.28, NE)
Median (95% CI)	NE (4.83, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.484 (0.328)
95% CI		(0.254, 0.922)
Log-rank p-value		0.054

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
Discontinuation due to TEAE
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.1 (81.8, 94.4)	92.7 (89.0, 96.4)
6 months	64.3 (44.6, 83.9)	84.2 (78.0, 90.3)
9 months	NE (NE, NE)	71.8 (62.2, 81.4)
12 months	NE (NE, NE)	71.8 (62.2, 81.4)
18 months	NE (NE, NE)	71.8 (62.2, 81.4)
Median Follow-up Time (months)	2.83	4.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
Discontinuation due to TEAE
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	32 (25.0)	61 (23.2)
Number of Subjects Censored, n (%)	96 (75.0)	202 (76.8)
Time to first TEAE (months)		
25% percentile (95% CI)	3.15 (1.28, NE)	5.39 (4.01, 8.90)
Median (95% CI)	NE (NE, NE)	NE (9.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.662 (0.224)
95% CI		(0.427, 1.028)
Log-rank p-value		0.072

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
Discontinuation due to TEAE
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.6 (68.0, 83.3)	81.9 (77.1, 86.6)
6 months	67.2 (53.7, 80.7)	74.5 (68.1, 80.9)
9 months	67.2 (53.7, 80.7)	64.8 (54.2, 75.3)
12 months	67.2 (53.7, 80.7)	55.9 (41.1, 70.6)
18 months	NE (NE, NE)	55.9 (41.1, 70.6)
Median Follow-up Time (months)	2.51	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
Deaths (Grade 5 TEAEs)
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	11 (10.8)	14 (7.3)
Number of Subjects Censored, n (%)	91 (89.2)	179 (92.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.87, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 8.4*	0.8, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.336 (0.436)
95% CI		(0.143, 0.790)
Log-rank p-value		0.014

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
Deaths (Grade 5 TEAEs)
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.5 (83.3, 95.7)	97.9 (95.9, 99.9)
6 months	86.7 (78.6, 94.8)	92.1 (87.4, 96.8)
9 months	NE (NE, NE)	86.1 (77.3, 94.9)
12 months	NE (NE, NE)	86.1 (77.3, 94.9)
18 months	NE (NE, NE)	86.1 (77.3, 94.9)
Median Follow-up Time (months)	2.83	4.93

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3E
Summary of Time to Onset of Overall TEAE by ECOG PS
Safety Population
Deaths (Grade 5 TEAEs)
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	34 (26.6)	34 (12.9)
Number of Subjects Censored, n (%)	94 (73.4)	229 (87.1)
Time to first TEAE (months)		
25% percentile (95% CI)	2.40 (1.68, NE)	12.22 (8.21, NE)
Median (95% CI)	NE (3.98, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.324 (0.253)
95% CI		(0.197, 0.531)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
TEAE
<= 18 months

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.6 (64.3, 80.8)	90.7 (87.0, 94.3)
6 months	64.0 (50.6, 77.5)	83.3 (77.3, 89.3)
9 months	64.0 (50.6, 77.5)	80.8 (73.3, 88.3)
12 months	64.0 (50.6, 77.5)	76.3 (65.2, 87.4)
18 months	NE (NE, NE)	65.4 (43.5, 87.4)
Median Follow-up Time (months)	2.58	3.25

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	12 (92.3)	35 (94.6)
Number of Subjects Censored, n (%)	1 (7.7)	2 (5.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.13 (0.03, 0.30)	0.23 (0.03, 0.26)
Median (95% CI)	0.30 (0.10, 0.69)	0.39 (0.26, 0.69)
75% percentile (95% CI)	0.69 (0.26, NE)	0.69 (0.56, 0.72)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
TEAE
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Min, Max	0.0, 3.7*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.000 (0.358)
95% CI		(0.496, 2.016)
Log-rank p-value		0.875

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
TEAE
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	7.7 (0.0, 22.2)	5.4 (0.0, 12.7)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.30	0.39

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
TEAE
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	201 (92.6)	416 (99.3)
Number of Subjects Censored, n (%)	16 (7.4)	3 (0.7)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.39, 0.59)	0.26 (0.20, 0.30)
75% percentile (95% CI)	0.72 (0.69, 0.82)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.425 (0.088)
95% CI		(1.200, 1.692)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
TEAE
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	7.7 (4.2, 11.3)	1.4 (0.3, 2.6)
6 months	NE (NE, NE)	0.4 (0.0, 1.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
Serious TEAE
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	7 (53.8)	7 (18.9)
Number of Subjects Censored, n (%)	6 (46.2)	30 (81.1)
Time to first TEAE (months)		
25% percentile (95% CI)	1.94 (0.23, 2.30)	4.57 (1.45, NE)
Median (95% CI)	2.30 (0.72, NE)	NE (4.57, NE)
75% percentile (95% CI)	4.14 (2.00, NE)	NE (NE, NE)
Min, Max	0.2, 4.1	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.234 (0.576)
95% CI		(0.076, 0.724)
Log-rank p-value		0.018

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
Serious TEAE
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	44.0 (12.9, 75.0)	83.8 (71.9, 95.7)
6 months	0.0 (NE, NE)	73.3 (51.5, 95.1)
9 months	0.0 (NE, NE)	73.3 (51.5, 95.1)
12 months	0.0 (NE, NE)	73.3 (51.5, 95.1)
18 months	0.0 (NE, NE)	73.3 (51.5, 95.1)
Median Follow-up Time (months)	1.94	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
Serious TEAE
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	81 (37.3)	164 (39.1)
Number of Subjects Censored, n (%)	136 (62.7)	255 (60.9)
Time to first TEAE (months)		
25% percentile (95% CI)	1.31 (0.99, 2.00)	2.66 (1.87, 3.19)
Median (95% CI)	NE (5.36, NE)	8.90 (7.03, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.718 (0.140)
95% CI		(0.546, 0.946)
Log-rank p-value		0.025

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
Serious TEAE
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	64.2 (57.7, 70.7)	71.3 (66.8, 75.7)
6 months	54.6 (44.1, 65.1)	57.9 (52.4, 63.4)
9 months	54.6 (44.1, 65.1)	49.3 (42.2, 56.5)
12 months	54.6 (44.1, 65.1)	40.6 (29.4, 51.9)
18 months	NE (NE, NE)	40.6 (29.4, 51.9)
Median Follow-up Time (months)	2.79	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
TEAE ≤ CTCAE Grade 2
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	11 (84.6)	34 (91.9)
Number of Subjects Censored, n (%)	2 (15.4)	3 (8.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.13 (0.03, 0.30)	0.23 (0.03, 0.33)
Median (95% CI)	0.30 (0.10, 0.69)	0.46 (0.26, 0.69)
75% percentile (95% CI)	0.69 (0.30, NE)	0.69 (0.66, 1.61)
Min, Max	0.0, 3.7*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.958 (0.369)
95% CI		(0.465, 1.973)
Log-rank p-value		0.706

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
TEAE ≤ CTCAE Grade 2
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	15.4 (0.0, 35.0)	6.8 (0.0, 15.4)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.30	0.46

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
TEAE ≤ CTCAE Grade 2
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	189 (87.1)	410 (97.9)
Number of Subjects Censored, n (%)	28 (12.9)	9 (2.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.56 (0.46, 0.69)	0.26 (0.23, 0.39)
75% percentile (95% CI)	0.76 (0.69, 1.25)	0.69 (NE, NE)
Min, Max	0.0, 4.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.467 (0.090)
95% CI		(1.231, 1.748)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
TEAE ≤ CTCAE Grade 2
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	11.1 (6.6, 15.5)	2.0 (0.6, 3.5)
6 months	NE (NE, NE)	0.5 (0.0, 1.4)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.56	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
TEAE ≥ CTCAE Grade 3
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	7 (53.8)	13 (35.1)
Number of Subjects Censored, n (%)	6 (46.2)	24 (64.9)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.23, 2.00)	1.51 (0.69, NE)
Median (95% CI)	2.00 (0.72, NE)	NE (4.57, NE)
75% percentile (95% CI)	4.14 (1.94, NE)	NE (NE, NE)
Min, Max	0.2, 4.1	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.550 (0.499)
95% CI		(0.207, 1.463)
Log-rank p-value		0.380

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
TEAE ≥ CTCAE Grade 3
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	46.2 (15.1, 77.2)	67.6 (52.5, 82.7)
6 months	0.0 (NE, NE)	57.9 (36.1, 79.7)
9 months	0.0 (NE, NE)	57.9 (36.1, 79.7)
12 months	0.0 (NE, NE)	57.9 (36.1, 79.7)
18 months	0.0 (NE, NE)	57.9 (36.1, 79.7)
Median Follow-up Time (months)	1.91	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
TEAE ≥ CTCAE Grade 3
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	109 (50.2)	273 (65.2)
Number of Subjects Censored, n (%)	108 (49.8)	146 (34.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.72, 1.25)	0.92 (0.69, 1.15)
Median (95% CI)	3.61 (2.27, 5.36)	2.69 (2.20, 3.25)
75% percentile (95% CI)	9.26 (5.55, NE)	8.38 (6.90, 11.96)
Min, Max	0.1, 9.3	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.142 (0.116)
95% CI		(0.909, 1.434)
Log-rank p-value		0.199

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
TEAE ≥ CTCAE Grade 3
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	54.4 (47.7, 61.1)	46.7 (41.9, 51.6)
6 months	33.2 (20.7, 45.7)	32.6 (27.4, 37.7)
9 months	33.2 (20.7, 45.7)	22.8 (16.5, 29.0)
12 months	0.0 (NE, NE)	15.9 (7.7, 24.2)
18 months	0.0 (NE, NE)	8.0 (0.0, 19.8)
Median Follow-up Time (months)	2.37	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
Discontinuation due to TEAE
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	3 (23.1)	3 (8.1)
Number of Subjects Censored, n (%)	10 (76.9)	34 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	4.57 (0.23, NE)	NE (NE, NE)
Median (95% CI)	4.57 (1.94, NE)	NE (NE, NE)
75% percentile (95% CI)	4.57 (NE, NE)	NE (NE, NE)
Min, Max	0.2, 4.6	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.282 (0.852)
95% CI		(0.053, 1.494)
Log-rank p-value		0.164

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
Discontinuation due to TEAE
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.1 (52.2, 100.0)	91.9 (83.1, 100.0)
6 months	0.0 (NE, NE)	91.9 (83.1, 100.0)
9 months	0.0 (NE, NE)	91.9 (83.1, 100.0)
12 months	0.0 (NE, NE)	91.9 (83.1, 100.0)
18 months	0.0 (NE, NE)	91.9 (83.1, 100.0)
Median Follow-up Time (months)	1.94	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
Discontinuation due to TEAE
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	46 (21.2)	90 (21.5)
Number of Subjects Censored, n (%)	171 (78.8)	329 (78.5)
Time to first TEAE (months)		
25% percentile (95% CI)	3.98 (3.15, NE)	7.03 (5.26, 8.38)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.630 (0.190)
95% CI		(0.434, 0.916)
Log-rank p-value		0.021

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
Discontinuation due to TEAE
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.2 (75.9, 86.5)	86.1 (82.7, 89.4)
6 months	67.1 (55.2, 79.1)	77.9 (73.2, 82.6)
9 months	67.1 (55.2, 79.1)	66.6 (59.2, 73.9)
12 months	67.1 (55.2, 79.1)	61.7 (52.1, 71.2)
18 months	NE (NE, NE)	61.7 (52.1, 71.2)
Median Follow-up Time (months)	2.83	3.98

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
Deaths (Grade 5 TEAEs)
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	2 (15.4)	4 (10.8)
Number of Subjects Censored, n (%)	11 (84.6)	33 (89.2)
Time to first TEAE (months)		
25% percentile (95% CI)	2.46 (2.30, NE)	NE (4.70, NE)
Median (95% CI)	NE (2.30, NE)	NE (4.70, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	1.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.557 (0.901)
95% CI		(0.095, 3.259)
Log-rank p-value		0.611

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
Deaths (Grade 5 TEAEs)
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.4 (38.0, 100.0)	91.8 (82.9, 100.0)
6 months	NE (NE, NE)	78.7 (53.7, 100.0)
9 months	NE (NE, NE)	78.7 (53.7, 100.0)
12 months	NE (NE, NE)	78.7 (53.7, 100.0)
18 months	NE (NE, NE)	78.7 (53.7, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3F
Summary of Time to Onset of Overall TEAE by Duration of Metastatic Disease
Safety Population
Deaths (Grade 5 TEAEs)
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	43 (19.8)	44 (10.5)
Number of Subjects Censored, n (%)	174 (80.2)	375 (89.5)
Time to first TEAE (months)		
25% percentile (95% CI)	3.98 (2.60, NE)	NE (9.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.6, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.313 (0.228)
95% CI		(0.200, 0.489)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE
Colon

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.4 (75.0, 85.9)	94.0 (91.7, 96.3)
6 months	74.6 (66.4, 82.9)	87.8 (83.9, 91.7)
9 months	74.6 (66.4, 82.9)	83.5 (77.7, 89.3)
12 months	74.6 (66.4, 82.9)	81.2 (74.0, 88.4)
18 months	NE (NE, NE)	75.4 (62.6, 88.2)
Median Follow-up Time (months)	2.83	4.24

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	130 (94.2)	273 (98.9)
Number of Subjects Censored, n (%)	8 (5.8)	3 (1.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.13 (0.07, 0.23)	0.10 (0.07, 0.10)
Median (95% CI)	0.46 (0.33, 0.59)	0.28 (0.23, 0.39)
75% percentile (95% CI)	0.69 (0.69, 0.76)	0.69 (0.66, 0.69)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.287 (0.108)
95% CI		(1.041, 1.593)
Log-rank p-value		0.019

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	6.3 (2.2, 10.4)	2.2 (0.5, 3.9)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.28

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	62 (89.9)	139 (98.6)
Number of Subjects Censored, n (%)	7 (10.1)	2 (1.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.23)	0.07 (0.07, 0.10)
Median (95% CI)	0.59 (0.26, 0.69)	0.26 (0.20, 0.36)
75% percentile (95% CI)	0.76 (0.69, 1.87)	0.69 (0.56, 0.69)
Min, Max	0.0, 3.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.500 (0.162)
95% CI		(1.091, 2.062)
Log-rank p-value		0.014

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	10.1 (3.0, 17.3)	1.4 (0.0, 3.4)
6 months	NE (NE, NE)	1.4 (0.0, 3.4)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.59	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	21 (91.3)	39 (100.0)
Number of Subjects Censored, n (%)	2 (8.7)	0
Time to first TEAE (months)		
25% percentile (95% CI)	0.03 (0.03, 0.36)	0.07 (0.03, 0.07)
Median (95% CI)	0.46 (0.07, 0.72)	0.13 (0.07, 0.39)
75% percentile (95% CI)	0.82 (0.46, 1.94)	0.66 (0.20, NE)
Min, Max	0.0, 2.9*	0.0, 0.7
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.141 (0.312)
95% CI		(1.161, 3.946)
Log-rank p-value		0.020

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	NE (NE, NE)	0.0 (NE, NE)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.46	0.13

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	53 (38.4)	104 (37.7)
Number of Subjects Censored, n (%)	85 (61.6)	172 (62.3)
Time to first TEAE (months)		
25% percentile (95% CI)	1.58 (0.99, 2.27)	2.66 (1.64, 3.25)
Median (95% CI)	5.36 (3.19, NE)	9.23 (6.90, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (11.96, NE)
Min, Max	0.2, 6.5*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.685 (0.177)
95% CI		(0.485, 0.969)
Log-rank p-value		0.028

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	62.1 (53.8, 70.5)	71.3 (65.8, 76.7)
6 months	46.5 (27.4, 65.7)	58.8 (51.8, 65.7)
9 months	NE (NE, NE)	50.3 (40.8, 59.7)
12 months	NE (NE, NE)	32.4 (13.7, 51.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.51	3.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	29 (42.0)	56 (39.7)
Number of Subjects Censored, n (%)	40 (58.0)	85 (60.3)
Time to first TEAE (months)		
25% percentile (95% CI)	1.25 (0.76, 1.38)	2.73 (1.84, 3.58)
Median (95% CI)	NE (2.04, NE)	8.28 (5.75, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.1, 13.0*	0.1, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.605 (0.239)
95% CI		(0.379, 0.966)
Log-rank p-value		0.057

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	62.1 (50.6, 73.6)	73.0 (65.6, 80.5)
6 months	50.2 (34.4, 66.0)	58.4 (49.2, 67.6)
9 months	50.2 (34.4, 66.0)	48.7 (37.1, 60.3)
12 months	50.2 (34.4, 66.0)	48.7 (37.1, 60.3)
18 months	NE (NE, NE)	48.7 (37.1, 60.3)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	6 (26.1)	11 (28.2)
Number of Subjects Censored, n (%)	17 (73.9)	28 (71.8)
Time to first TEAE (months)		
25% percentile (95% CI)	2.00 (0.16, NE)	4.07 (0.92, NE)
Median (95% CI)	NE (NE, NE)	NE (5.95, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.968 (0.525)
95% CI		(0.346, 2.706)
Log-rank p-value		0.958

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.7 (55.5, 91.8)	76.4 (62.8, 89.9)
6 months	73.7 (55.5, 91.8)	64.8 (45.9, 83.6)
9 months	NE (NE, NE)	64.8 (45.9, 83.6)
12 months	NE (NE, NE)	64.8 (45.9, 83.6)
18 months	NE (NE, NE)	64.8 (45.9, 83.6)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≤ CTCAE Grade 2
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	119 (86.2)	268 (97.1)
Number of Subjects Censored, n (%)	19 (13.8)	8 (2.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.13 (0.07, 0.23)	0.10 (0.07, 0.10)
Median (95% CI)	0.51 (0.36, 0.69)	0.36 (0.26, 0.46)
75% percentile (95% CI)	0.72 (0.69, 1.02)	0.69 (0.69, 0.72)
Min, Max	0.0, 4.7*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.364 (0.112)
95% CI		(1.096, 1.698)
Log-rank p-value		0.010

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≤ CTCAE Grade 2
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	12.4 (6.5, 18.2)	3.1 (0.9, 5.3)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.51	0.36

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≤ CTCAE Grade 2
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	60 (87.0)	137 (97.2)
Number of Subjects Censored, n (%)	9 (13.0)	4 (2.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.23)	0.10 (0.07, 0.13)
Median (95% CI)	0.59 (0.30, 0.69)	0.26 (0.23, 0.39)
75% percentile (95% CI)	0.95 (0.69, 1.87)	0.69 (0.66, 0.69)
Min, Max	0.0, 3.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.461 (0.163)
95% CI		(1.060, 2.012)
Log-rank p-value		0.022

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≤ CTCAE Grade 2
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	11.3 (3.6, 19.0)	1.7 (0.0, 3.9)
6 months	NE (NE, NE)	1.7 (0.0, 3.9)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.59	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≤ CTCAE Grade 2
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	21 (91.3)	39 (100.0)
Number of Subjects Censored, n (%)	2 (8.7)	0
Time to first TEAE (months)		
25% percentile (95% CI)	0.03 (0.03, 0.36)	0.07 (0.03, 0.07)
Median (95% CI)	0.46 (0.07, 0.72)	0.13 (0.07, 0.39)
75% percentile (95% CI)	0.82 (0.46, 1.94)	0.66 (0.20, NE)
Min, Max	0.0, 2.9*	0.0, 0.7
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.141 (0.312)
95% CI		(1.161, 3.946)
Log-rank p-value		0.020

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≤ CTCAE Grade 2
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	NE (NE, NE)	0.0 (NE, NE)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.46	0.13

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≥ CTCAE Grade 3
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	67 (48.6)	174 (63.0)
Number of Subjects Censored, n (%)	71 (51.4)	102 (37.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.99 (0.72, 1.38)	0.89 (0.69, 1.25)
Median (95% CI)	3.61 (2.23, NE)	2.79 (1.91, 3.91)
75% percentile (95% CI)	NE (5.36, NE)	8.90 (6.90, NE)
Min, Max	0.2, 6.5*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.180 (0.148)
95% CI		(0.883, 1.577)
Log-rank p-value		0.282

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≥ CTCAE Grade 3
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	53.4 (45.0, 61.9)	48.0 (42.0, 53.9)
6 months	37.7 (21.2, 54.1)	34.2 (27.6, 40.8)
9 months	NE (NE, NE)	23.8 (15.5, 32.1)
12 months	NE (NE, NE)	11.4 (0.0, 22.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	2.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≥ CTCAE Grade 3
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	37 (53.6)	90 (63.8)
Number of Subjects Censored, n (%)	32 (46.4)	51 (36.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.92 (0.66, 1.25)	1.15 (0.69, 1.51)
Median (95% CI)	3.35 (1.28, 4.83)	3.25 (2.37, 3.98)
75% percentile (95% CI)	9.26 (4.14, NE)	7.62 (5.59, NE)
Min, Max	0.1, 9.3	0.1, 16.1
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.946 (0.205)
95% CI		(0.633, 1.413)
Log-rank p-value		0.968

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≥ CTCAE Grade 3
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	56.4 (44.6, 68.1)	50.3 (41.9, 58.6)
6 months	27.4 (8.9, 45.9)	33.2 (24.3, 42.2)
9 months	27.4 (8.9, 45.9)	23.9 (13.7, 34.0)
12 months	0.0 (NE, NE)	23.9 (13.7, 34.0)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.27	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≥ CTCAE Grade 3
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	12 (52.2)	22 (56.4)
Number of Subjects Censored, n (%)	11 (47.8)	17 (43.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.62 (0.16, 1.87)	0.69 (0.53, 1.31)
Median (95% CI)	5.55 (1.61, NE)	2.53 (1.15, NE)
75% percentile (95% CI)	NE (5.55, NE)	NE (3.19, NE)
Min, Max	0.2, 6.8*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.162 (0.378)
95% CI		(0.554, 2.438)
Log-rank p-value		0.730

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≥ CTCAE Grade 3
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	51.8 (31.2, 72.4)	45.0 (29.1, 60.9)
6 months	25.9 (0.0, 63.3)	40.0 (23.1, 56.9)
9 months	NE (NE, NE)	40.0 (23.1, 56.9)
12 months	NE (NE, NE)	40.0 (23.1, 56.9)
18 months	NE (NE, NE)	40.0 (23.1, 56.9)
Median Follow-up Time (months)	2.00	1.91

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
Discontinuation due to TEAE
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	27 (19.6)	63 (22.8)
Number of Subjects Censored, n (%)	111 (80.4)	213 (77.2)
Time to first TEAE (months)		
25% percentile (95% CI)	3.65 (1.81, NE)	5.72 (4.27, 8.21)
Median (95% CI)	NE (NE, NE)	NE (8.90, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.721 (0.245)
95% CI		(0.446, 1.164)
Log-rank p-value		0.165

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
Discontinuation due to TEAE
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.5 (74.9, 88.0)	86.6 (82.5, 90.7)
6 months	74.3 (63.0, 85.6)	74.3 (67.7, 80.9)
9 months	NE (NE, NE)	60.7 (50.1, 71.3)
12 months	NE (NE, NE)	51.4 (36.2, 66.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
Discontinuation due to TEAE
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	19 (27.5)	24 (17.0)
Number of Subjects Censored, n (%)	50 (72.5)	117 (83.0)
Time to first TEAE (months)		
25% percentile (95% CI)	3.98 (1.28, 4.57)	NE (6.18, NE)
Median (95% CI)	4.83 (4.34, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (4.83, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.414 (0.327)
95% CI		(0.219, 0.786)
Log-rank p-value		0.015

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
Discontinuation due to TEAE
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.1 (69.3, 88.9)	86.9 (81.3, 92.6)
6 months	47.6 (24.4, 70.9)	84.5 (78.1, 91.0)
9 months	47.6 (24.4, 70.9)	75.2 (64.6, 85.7)
12 months	47.6 (24.4, 70.9)	75.2 (64.6, 85.7)
18 months	NE (NE, NE)	75.2 (64.6, 85.7)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
Discontinuation due to TEAE
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	3 (13.0)	6 (15.4)
Number of Subjects Censored, n (%)	20 (87.0)	33 (84.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.23, NE)	NE (0.89, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.080 (0.731)
95% CI		(0.258, 4.523)
Log-rank p-value		0.896

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
Discontinuation due to TEAE
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.0 (73.2, 100.0)	84.6 (73.3, 95.9)
6 months	87.0 (73.2, 100.0)	84.6 (73.3, 95.9)
9 months	NE (NE, NE)	84.6 (73.3, 95.9)
12 months	NE (NE, NE)	84.6 (73.3, 95.9)
18 months	NE (NE, NE)	84.6 (73.3, 95.9)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
Deaths (Grade 5 TEAEs)
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	31 (22.5)	32 (11.6)
Number of Subjects Censored, n (%)	107 (77.5)	244 (88.4)
Time to first TEAE (months)		
25% percentile (95% CI)	3.19 (2.27, NE)	12.22 (9.69, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 6.8*	0.8, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.300 (0.271)
95% CI		(0.176, 0.511)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
Deaths (Grade 5 TEAEs)
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.4 (70.1, 84.7)	93.5 (90.5, 96.5)
6 months	70.4 (58.8, 82.0)	85.5 (80.1, 90.9)
9 months	NE (NE, NE)	83.1 (76.9, 89.3)
12 months	NE (NE, NE)	78.5 (67.9, 89.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
Deaths (Grade 5 TEAEs)
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	11 (15.9)	13 (9.2)
Number of Subjects Censored, n (%)	58 (84.1)	128 (90.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.33, NE)	NE (8.87, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.6, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.431 (0.438)
95% CI		(0.183, 1.017)
Log-rank p-value		0.080

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
Deaths (Grade 5 TEAEs)
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.0 (76.3, 93.6)	94.2 (90.2, 98.1)
6 months	78.4 (63.8, 93.1)	90.7 (85.3, 96.1)
9 months	78.4 (63.8, 93.1)	84.1 (73.8, 94.4)
12 months	78.4 (63.8, 93.1)	84.1 (73.8, 94.4)
18 months	NE (NE, NE)	84.1 (73.8, 94.4)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3G
Summary of Time to Onset of Overall TEAE by Primary Tumor Site at 1st Diagnosis
Safety Population
Deaths (Grade 5 TEAEs)
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	3 (13.0)	3 (7.7)
Number of Subjects Censored, n (%)	20 (87.0)	36 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.48, NE)	NE (5.95, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.9, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.630 (0.868)
95% CI		(0.115, 3.451)
Log-rank p-value		0.686

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.8 (69.0, 100.0)	94.9 (87.9, 100.0)
6 months	84.8 (69.0, 100.0)	87.6 (72.4, 100.0)
9 months	NE (NE, NE)	87.6 (72.4, 100.0)
12 months	NE (NE, NE)	87.6 (72.4, 100.0)
18 months	NE (NE, NE)	87.6 (72.4, 100.0)
Median Follow-up Time (months)	2.83	3.02

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	82 (96.5)	167 (98.8)
Number of Subjects Censored, n (%)	3 (3.5)	2 (1.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.13)	0.07 (0.07, 0.10)
Median (95% CI)	0.39 (0.20, 0.59)	0.23 (0.16, 0.36)
75% percentile (95% CI)	0.69 (0.66, 0.76)	0.69 (0.62, 0.69)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Min, Max	0.0, 3.6	0.0, 5.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.173 (0.136)
95% CI		(0.898, 1.533)
Log-rank p-value		0.261

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	4.7 (0.2, 9.2)	2.4 (0.1, 4.7)
6 months	0.0 (NE, NE)	0.0 (NE, NE)
9 months	0.0 (NE, NE)	0.0 (NE, NE)
12 months	0.0 (NE, NE)	0.0 (NE, NE)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.39	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
TEAE
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	131 (90.3)	284 (99.0)
Number of Subjects Censored, n (%)	14 (9.7)	3 (1.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.16 (0.07, 0.26)	0.07 (0.07, 0.10)
Median (95% CI)	0.56 (0.39, 0.69)	0.26 (0.23, 0.36)
75% percentile (95% CI)	0.72 (0.69, 1.15)	0.69 (0.62, 0.69)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.581 (0.108)
95% CI		(1.279, 1.955)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
TEAE
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	9.5 (4.7, 14.3)	1.4 (0.0, 2.8)
6 months	NE (NE, NE)	0.9 (0.0, 2.1)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.56	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
Serious TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	31 (36.5)	64 (37.9)
Number of Subjects Censored, n (%)	54 (63.5)	105 (62.1)
Time to first TEAE (months)		
25% percentile (95% CI)	2.00 (0.95, 3.19)	2.83 (1.68, 3.98)
Median (95% CI)	4.14 (3.19, NE)	9.23 (7.03, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (11.96, NE)
Min, Max	0.2, 6.8*	0.1, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.716 (0.226)
95% CI		(0.459, 1.116)
Log-rank p-value		0.205

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
Serious TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	68.4 (58.3, 78.5)	72.7 (65.9, 79.6)
6 months	49.9 (33.5, 66.3)	59.2 (50.6, 67.8)
9 months	NE (NE, NE)	52.5 (42.1, 63.0)
12 months	NE (NE, NE)	35.5 (13.0, 57.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.52

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
Serious TEAE
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	57 (39.3)	107 (37.3)
Number of Subjects Censored, n (%)	88 (60.7)	180 (62.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.22 (0.76, 1.64)	2.53 (1.84, 3.29)
Median (95% CI)	NE (5.36, NE)	8.90 (6.90, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.687 (0.170)
95% CI		(0.493, 0.959)
Log-rank p-value		0.028

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
Serious TEAE
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	60.4 (52.3, 68.5)	72.0 (66.6, 77.3)
6 months	53.7 (39.3, 68.0)	58.9 (52.1, 65.7)
9 months	53.7 (39.3, 68.0)	49.7 (40.6, 58.7)
12 months	53.7 (39.3, 68.0)	45.5 (34.2, 56.9)
18 months	NE (NE, NE)	45.5 (34.2, 56.9)
Median Follow-up Time (months)	2.46	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
TEAE ≤ CTCAE Grade 2
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	76 (89.4)	167 (98.8)
Number of Subjects Censored, n (%)	9 (10.6)	2 (1.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.13)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.20, 0.66)	0.23 (0.16, 0.39)
75% percentile (95% CI)	0.72 (0.69, 1.02)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.7*	0.0, 5.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.308 (0.140)
95% CI		(0.994, 1.722)
Log-rank p-value		0.072

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
TEAE ≤ CTCAE Grade 2
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	9.6 (3.0, 16.2)	2.4 (0.1, 4.7)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.46	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
TEAE ≤ CTCAE Grade 2
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	124 (85.5)	277 (96.5)
Number of Subjects Censored, n (%)	21 (14.5)	10 (3.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.16 (0.07, 0.30)	0.10 (0.07, 0.13)
Median (95% CI)	0.59 (0.46, 0.69)	0.33 (0.26, 0.43)
75% percentile (95% CI)	0.95 (0.69, 1.64)	0.69 (NE, NE)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.530 (0.110)
95% CI		(1.232, 1.900)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
TEAE ≤ CTCAE Grade 2
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	12.6 (7.0, 18.3)	2.4 (0.4, 4.4)
6 months	NE (NE, NE)	1.6 (0.0, 3.5)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.59	0.33

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
TEAE ≥ CTCAE Grade 3
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	44 (51.8)	108 (63.9)
Number of Subjects Censored, n (%)	41 (48.2)	61 (36.1)
Time to first TEAE (months)		
25% percentile (95% CI)	1.25 (0.72, 1.87)	1.15 (0.69, 1.51)
Median (95% CI)	3.35 (2.00, 4.83)	3.19 (2.53, 4.04)
75% percentile (95% CI)	NE (4.14, NE)	7.39 (5.95, NE)
Min, Max	0.1, 6.8*	0.1, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.046 (0.182)
95% CI		(0.732, 1.495)
Log-rank p-value		0.739

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
TEAE ≥ CTCAE Grade 3
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	55.8 (45.1, 66.5)	51.5 (43.8, 59.1)
6 months	33.1 (17.9, 48.3)	31.2 (22.7, 39.7)
9 months	NE (NE, NE)	24.0 (15.0, 33.1)
12 months	NE (NE, NE)	9.6 (0.0, 24.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.40	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
TEAE ≥ CTCAE Grade 3
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	72 (49.7)	178 (62.0)
Number of Subjects Censored, n (%)	73 (50.3)	109 (38.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.69, 1.22)	0.92 (0.69, 1.15)
Median (95% CI)	4.34 (1.94, NE)	2.60 (1.87, 3.61)
75% percentile (95% CI)	9.26 (5.36, NE)	11.04 (7.46, NE)
Min, Max	0.1, 9.3	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.129 (0.143)
95% CI		(0.854, 1.495)
Log-rank p-value		0.344

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
TEAE ≥ CTCAE Grade 3
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	53.2 (45.0, 61.4)	46.6 (40.7, 52.4)
6 months	31.1 (12.0, 50.2)	36.2 (29.9, 42.4)
9 months	31.1 (12.0, 50.2)	25.5 (17.3, 33.6)
12 months	0.0 (NE, NE)	22.3 (13.1, 31.5)
18 months	0.0 (NE, NE)	14.9 (1.5, 28.2)
Median Follow-up Time (months)	2.27	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
Discontinuation due to TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	21 (24.7)	32 (18.9)
Number of Subjects Censored, n (%)	64 (75.3)	137 (81.1)
Time to first TEAE (months)		
25% percentile (95% CI)	3.65 (1.81, 4.83)	7.52 (5.03, NE)
Median (95% CI)	NE (3.98, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.525 (0.293)
95% CI		(0.296, 0.934)
Log-rank p-value		0.036

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
Discontinuation due to TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.9 (73.6, 90.2)	86.0 (80.7, 91.3)
6 months	52.4 (31.5, 73.4)	79.4 (72.2, 86.6)
9 months	NE (NE, NE)	74.9 (65.9, 84.0)
12 months	NE (NE, NE)	69.2 (55.5, 82.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.07

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
Discontinuation due to TEAE
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	28 (19.3)	61 (21.3)
Number of Subjects Censored, n (%)	117 (80.7)	226 (78.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.61, NE)	6.90 (4.76, 8.38)
Median (95% CI)	NE (NE, NE)	NE (11.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.718 (0.238)
95% CI		(0.450, 1.146)
Log-rank p-value		0.169

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
Discontinuation due to TEAE
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.0 (74.6, 87.5)	86.9 (82.9, 90.8)
6 months	76.3 (65.4, 87.2)	78.2 (72.4, 84.0)
9 months	76.3 (65.4, 87.2)	63.2 (53.2, 73.1)
12 months	76.3 (65.4, 87.2)	58.6 (46.1, 71.2)
18 months	NE (NE, NE)	58.6 (46.1, 71.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
Deaths (Grade 5 TEAEs)
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	20 (23.5)	14 (8.3)
Number of Subjects Censored, n (%)	65 (76.5)	155 (91.7)
Time to first TEAE (months)		
25% percentile (95% CI)	3.75 (2.37, NE)	NE (9.69, NE)
Median (95% CI)	NE (3.98, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.9, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.224 (0.371)
95% CI		(0.108, 0.465)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
Deaths (Grade 5 TEAEs)
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.5 (69.3, 87.6)	94.4 (90.8, 98.0)
6 months	66.2 (50.9, 81.4)	89.8 (84.3, 95.4)
9 months	NE (NE, NE)	89.8 (84.3, 95.4)
12 months	NE (NE, NE)	82.9 (68.9, 96.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3H
Summary of Time to Onset of Overall TEAE by RAS Status
Safety Population
Deaths (Grade 5 TEAEs)
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	25 (17.2)	34 (11.8)
Number of Subjects Censored, n (%)	120 (82.8)	253 (88.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.30, NE)	12.22 (8.21, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.437 (0.277)
95% CI		(0.254, 0.751)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.6 (75.0, 88.2)	93.5 (90.6, 96.4)
6 months	81.6 (75.0, 88.2)	85.9 (80.7, 91.1)
9 months	81.6 (75.0, 88.2)	79.5 (71.3, 87.6)
12 months	81.6 (75.0, 88.2)	79.5 (71.3, 87.6)
18 months	NE (NE, NE)	69.5 (50.0, 89.1)
Median Follow-up Time (months)	2.83	3.75

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	182 (92.4)	393 (99.0)
Number of Subjects Censored, n (%)	15 (7.6)	4 (1.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.10 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.33, 0.59)	0.26 (0.23, 0.33)
75% percentile (95% CI)	0.69 (0.69, 0.82)	0.69 (0.66, 0.69)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.410 (0.092)
95% CI		(1.179, 1.687)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	8.0 (4.2, 11.8)	1.5 (0.3, 2.7)
6 months	NE (NE, NE)	0.8 (0.0, 1.7)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
TEAE
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	10 (100.0)	7 (100.0)
Number of Subjects Censored, n (%)	0	0
Time to first TEAE (months)		
25% percentile (95% CI)	0.03 (0.03, 0.69)	0.26 (0.03, 0.69)
Median (95% CI)	0.67 (0.03, 0.76)	0.69 (0.03, 0.72)
75% percentile (95% CI)	0.76 (0.66, NE)	0.72 (0.62, NE)
Min, Max	0.0, 1.0	0.0, 1.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.693 (0.640)
95% CI		(0.198, 2.428)
Log-rank p-value		0.513

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
TEAE
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	0.0 (NE, NE)	0.0 (NE, NE)
6 months	0.0 (NE, NE)	0.0 (NE, NE)
9 months	0.0 (NE, NE)	0.0 (NE, NE)
12 months	0.0 (NE, NE)	0.0 (NE, NE)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.67	0.69

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
TEAE
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	21 (91.3)	51 (98.1)
Number of Subjects Censored, n (%)	2 (8.7)	1 (1.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.46)	0.07 (0.07, 0.16)
Median (95% CI)	0.53 (0.07, 0.72)	0.26 (0.16, 0.39)
75% percentile (95% CI)	1.02 (0.69, 1.87)	0.69 (0.39, 0.82)
Min, Max	0.0, 3.4*	0.0, 3.7
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.508 (0.278)
95% CI		(0.875, 2.600)
Log-rank p-value		0.162

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
TEAE
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	8.7 (0.0, 20.2)	3.8 (0.0, 9.1)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.53	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
Serious TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	80 (40.6)	147 (37.0)
Number of Subjects Censored, n (%)	117 (59.4)	250 (63.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.22 (0.92, 1.68)	2.83 (2.00, 3.25)
Median (95% CI)	5.36 (3.35, NE)	8.90 (7.75, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.622 (0.143)
95% CI		(0.470, 0.823)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
Serious TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	61.4 (54.4, 68.3)	72.6 (68.1, 77.1)
6 months	48.5 (36.9, 60.1)	59.2 (53.5, 64.9)
9 months	NE (NE, NE)	49.8 (41.9, 57.7)
12 months	NE (NE, NE)	39.3 (26.4, 52.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
Serious TEAE
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	3 (30.0)	3 (42.9)
Number of Subjects Censored, n (%)	7 (70.0)	4 (57.1)
Time to first TEAE (months)		
25% percentile (95% CI)	2.00 (0.49, NE)	0.79 (0.72, NE)
Median (95% CI)	NE (0.49, NE)	7.03 (0.72, NE)
75% percentile (95% CI)	NE (NE, NE)	7.03 (NE, NE)
Min, Max	0.5, 13.0*	0.7, 7.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.034 (0.979)
95% CI		(0.152, 7.043)
Log-rank p-value		0.692

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
Serious TEAE
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	70.0 (41.6, 98.4)	71.4 (38.0, 100.0)
6 months	70.0 (41.6, 98.4)	71.4 (38.0, 100.0)
9 months	70.0 (41.6, 98.4)	0.0 (NE, NE)
12 months	70.0 (41.6, 98.4)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.81	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
Serious TEAE
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	5 (21.7)	21 (40.4)
Number of Subjects Censored, n (%)	18 (78.3)	31 (59.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.66, NE)	2.07 (0.95, 5.72)
Median (95% CI)	NE (NE, NE)	18.04 (4.50, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.7, 6.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.737 (0.541)
95% CI		(0.601, 5.017)
Log-rank p-value		0.305

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
Serious TEAE
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.7 (60.5, 95.0)	69.0 (56.3, 81.6)
6 months	77.7 (60.5, 95.0)	55.3 (39.6, 71.1)
9 months	NE (NE, NE)	55.3 (39.6, 71.1)
12 months	NE (NE, NE)	55.3 (39.6, 71.1)
18 months	NE (NE, NE)	55.3 (39.6, 71.1)
Median Follow-up Time (months)	2.86	3.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
TEAE ≤ CTCAE Grade 2
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	169 (85.8)	388 (97.7)
Number of Subjects Censored, n (%)	28 (14.2)	9 (2.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.10 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.53 (0.39, 0.66)	0.30 (0.23, 0.39)
75% percentile (95% CI)	0.76 (0.69, 1.35)	0.69 (NE, NE)
Min, Max	0.0, 4.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.474 (0.094)
95% CI		(1.227, 1.772)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
TEAE ≤ CTCAE Grade 2
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	12.3 (7.5, 17.2)	2.0 (0.5, 3.5)
6 months	NE (NE, NE)	1.0 (0.0, 2.2)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.53	0.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
TEAE ≤ CTCAE Grade 2
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	10 (100.0)	7 (100.0)
Number of Subjects Censored, n (%)	0	0
Time to first TEAE (months)		
25% percentile (95% CI)	0.03 (0.03, 0.69)	0.26 (0.03, 0.69)
Median (95% CI)	0.67 (0.03, 0.76)	0.69 (0.03, 0.95)
75% percentile (95% CI)	0.76 (0.66, NE)	0.95 (0.66, NE)
Min, Max	0.0, 1.0	0.0, 1.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.609 (0.654)
95% CI		(0.169, 2.196)
Log-rank p-value		0.513

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
TEAE ≤ CTCAE Grade 2
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	0.0 (NE, NE)	0.0 (NE, NE)
6 months	0.0 (NE, NE)	0.0 (NE, NE)
9 months	0.0 (NE, NE)	0.0 (NE, NE)
12 months	0.0 (NE, NE)	0.0 (NE, NE)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.67	0.69

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
TEAE ≤ CTCAE Grade 2
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	21 (91.3)	49 (94.2)
Number of Subjects Censored, n (%)	2 (8.7)	3 (5.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.46)	0.07 (0.07, 0.16)
Median (95% CI)	0.53 (0.07, 0.72)	0.26 (0.16, 0.53)
75% percentile (95% CI)	1.02 (0.69, 1.87)	0.71 (0.53, 0.85)
Min, Max	0.0, 3.4*	0.0, 3.7
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.353 (0.280)
95% CI		(0.782, 2.341)
Log-rank p-value		0.266

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
TEAE ≤ CTCAE Grade 2
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	8.7 (0.0, 20.2)	6.3 (0.0, 13.0)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.53	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
TEAE ≥ CTCAE Grade 3
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	103 (52.3)	249 (62.7)
Number of Subjects Censored, n (%)	94 (47.7)	148 (37.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.92 (0.72, 1.12)	0.95 (0.69, 1.18)
Median (95% CI)	3.35 (2.00, 4.34)	2.83 (2.43, 3.58)
75% percentile (95% CI)	NE (4.83, NE)	8.38 (7.33, 11.96)
Min, Max	0.1, 6.8*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.027 (0.119)
95% CI		(0.813, 1.297)
Log-rank p-value		0.660

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
TEAE ≥ CTCAE Grade 3
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	52.6 (45.6, 59.7)	48.3 (43.3, 53.3)
6 months	27.7 (14.7, 40.7)	33.3 (27.8, 38.8)
9 months	NE (NE, NE)	22.7 (15.5, 29.9)
12 months	NE (NE, NE)	13.5 (3.7, 23.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	2.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
TEAE ≥ CTCAE Grade 3
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	5 (50.0)	5 (71.4)
Number of Subjects Censored, n (%)	5 (50.0)	2 (28.6)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.49, NE)	0.72 (0.62, 0.95)
Median (95% CI)	9.26 (0.49, NE)	0.95 (0.62, NE)
75% percentile (95% CI)	9.26 (NE, NE)	6.90 (0.79, NE)
Min, Max	0.5, 9.3	0.6, 7.0*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.193 (0.885)
95% CI		(0.210, 6.765)
Log-rank p-value		0.862

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
TEAE ≥ CTCAE Grade 3
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	60.0 (29.6, 90.4)	42.9 (6.2, 79.5)
6 months	60.0 (29.6, 90.4)	42.9 (6.2, 79.5)
9 months	60.0 (29.6, 90.4)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	0.95

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
TEAE ≥ CTCAE Grade 3
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	8 (34.8)	32 (61.5)
Number of Subjects Censored, n (%)	15 (65.2)	20 (38.5)
Time to first TEAE (months)		
25% percentile (95% CI)	1.61 (0.62, NE)	1.28 (0.62, 1.64)
Median (95% CI)	NE (1.64, NE)	2.69 (1.64, 7.10)
75% percentile (95% CI)	NE (NE, NE)	16.07 (5.55, NE)
Min, Max	0.6, 6.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.741 (0.427)
95% CI		(0.755, 4.018)
Log-rank p-value		0.292

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
TEAE ≥ CTCAE Grade 3
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	64.9 (45.3, 84.6)	49.7 (36.1, 63.4)
6 months	64.9 (45.3, 84.6)	38.3 (23.8, 52.7)
9 months	NE (NE, NE)	34.4 (19.6, 49.3)
12 months	NE (NE, NE)	34.4 (19.6, 49.3)
18 months	NE (NE, NE)	23.0 (2.1, 43.8)
Median Follow-up Time (months)	2.83	2.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
Discontinuation due to TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	46 (23.4)	80 (20.2)
Number of Subjects Censored, n (%)	151 (76.6)	317 (79.8)
Time to first TEAE (months)		
25% percentile (95% CI)	3.65 (1.81, 4.83)	7.46 (5.32, 8.90)
Median (95% CI)	NE (4.83, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.563 (0.194)
95% CI		(0.385, 0.823)
Log-rank p-value		0.004

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
Discontinuation due to TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.6 (73.9, 85.4)	86.3 (82.9, 89.8)
6 months	60.9 (47.1, 74.7)	79.2 (74.4, 83.9)
9 months	NE (NE, NE)	66.6 (58.4, 74.8)
12 months	NE (NE, NE)	63.1 (52.9, 73.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
Discontinuation due to TEAE
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	1 (10.0)	3 (42.9)
Number of Subjects Censored, n (%)	9 (90.0)	4 (57.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.49, NE)	4.11 (0.79, NE)
Median (95% CI)	NE (0.49, NE)	7.03 (0.79, NE)
75% percentile (95% CI)	NE (NE, NE)	7.03 (NE, NE)
Min, Max	0.5, 13.0*	0.8, 7.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.773 (1.591)
95% CI		(0.034, 17.480)
Log-rank p-value		0.808

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
Discontinuation due to TEAE
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (71.4, 100.0)	85.7 (59.8, 100.0)
6 months	90.0 (71.4, 100.0)	71.4 (38.0, 100.0)
9 months	90.0 (71.4, 100.0)	0.0 (NE, NE)
12 months	90.0 (71.4, 100.0)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.81	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
Discontinuation due to TEAE
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	2 (8.7)	10 (19.2)
Number of Subjects Censored, n (%)	21 (91.3)	42 (80.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.66, NE)	9.69 (4.17, NE)
Median (95% CI)	NE (NE, NE)	NE (9.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.4*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.536 (0.847)
95% CI		(0.292, 8.081)
Log-rank p-value		0.438

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
Discontinuation due to TEAE
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (79.8, 100.0)	88.3 (79.4, 97.1)
6 months	91.3 (79.8, 100.0)	76.9 (62.6, 91.2)
9 months	NE (NE, NE)	76.9 (62.6, 91.2)
12 months	NE (NE, NE)	69.2 (50.0, 88.5)
18 months	NE (NE, NE)	69.2 (50.0, 88.5)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
Deaths (Grade 5 TEAEs)
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	40 (20.3)	36 (9.1)
Number of Subjects Censored, n (%)	157 (79.7)	361 (90.9)
Time to first TEAE (months)		
25% percentile (95% CI)	3.98 (2.46, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.6, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.302 (0.239)
95% CI		(0.189, 0.482)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
Deaths (Grade 5 TEAEs)
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.7 (73.7, 85.6)	94.2 (91.8, 96.6)
6 months	73.1 (64.1, 82.2)	88.9 (85.1, 92.7)
9 months	NE (NE, NE)	84.5 (78.2, 90.9)
12 months	NE (NE, NE)	84.5 (78.2, 90.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
Deaths (Grade 5 TEAEs)
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	2 (20.0)	0
Number of Subjects Censored, n (%)	8 (80.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.82, NE)	NE (NE, NE)
Median (95% CI)	NE (0.82, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8, 13.0*	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.274

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
Deaths (Grade 5 TEAEs)
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.0 (55.2, 100.0)	100.0 (100.0, 100.0)
6 months	80.0 (55.2, 100.0)	100.0 (100.0, 100.0)
9 months	80.0 (55.2, 100.0)	NE (NE, NE)
12 months	80.0 (55.2, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3I
Summary of Time to Onset of Overall TEAE by BRAF Status
Safety Population
Deaths (Grade 5 TEAEs)
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	3 (13.0)	12 (23.1)
Number of Subjects Censored, n (%)	20 (87.0)	40 (76.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.64, NE)	6.18 (4.27, 12.22)
Median (95% CI)	NE (NE, NE)	12.22 (9.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (12.22, NE)
Min, Max	1.6, 6.4*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.645 (0.779)
95% CI		(0.357, 7.573)
Log-rank p-value		0.733

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE
<=3

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.3 (71.9, 100.0)	90.3 (82.1, 98.4)
6 months	86.3 (71.9, 100.0)	75.2 (60.1, 90.4)
9 months	NE (NE, NE)	71.1 (54.7, 87.4)
12 months	NE (NE, NE)	64.0 (44.2, 83.7)
18 months	NE (NE, NE)	48.0 (17.0, 78.9)
Median Follow-up Time (months)	2.86	3.76

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	39 (86.7)	73 (96.1)
Number of Subjects Censored, n (%)	6 (13.3)	3 (3.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.36)	0.13 (0.07, 0.23)
Median (95% CI)	0.66 (0.30, 0.69)	0.39 (0.23, 0.66)
75% percentile (95% CI)	1.28 (0.69, 3.65)	0.72 (0.66, 0.95)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.346 (0.210)
95% CI		(0.892, 2.032)
Log-rank p-value		0.126

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	15.6 (5.0, 26.1)	5.3 (0.2, 10.3)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.66	0.39

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	174 (94.1)	378 (99.5)
Number of Subjects Censored, n (%)	11 (5.9)	2 (0.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.10 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.33, 0.56)	0.25 (0.20, 0.30)
75% percentile (95% CI)	0.69 (0.69, 0.76)	0.69 (0.62, 0.69)
Min, Max	0.0, 3.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.398 (0.093)
95% CI		(1.165, 1.678)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	5.8 (2.4, 9.2)	1.1 (0.0, 2.1)
6 months	NE (NE, NE)	0.4 (0.0, 1.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
Serious TEAE
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	14 (31.1)	27 (35.5)
Number of Subjects Censored, n (%)	31 (68.9)	49 (64.5)
Time to first TEAE (months)		
25% percentile (95% CI)	2.00 (0.89, NE)	2.73 (1.48, 5.32)
Median (95% CI)	NE (3.65, NE)	9.23 (5.32, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.855 (0.355)
95% CI		(0.427, 1.715)
Log-rank p-value		0.791

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
Serious TEAE
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	70.5 (57.0, 84.0)	73.3 (63.3, 83.4)
6 months	NE (NE, NE)	63.0 (50.0, 75.9)
9 months	NE (NE, NE)	54.0 (38.0, 70.0)
12 months	NE (NE, NE)	48.0 (29.9, 66.0)
18 months	NE (NE, NE)	48.0 (29.9, 66.0)
Median Follow-up Time (months)	2.83	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
Serious TEAE
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	74 (40.0)	144 (37.9)
Number of Subjects Censored, n (%)	111 (60.0)	236 (62.1)
Time to first TEAE (months)		
25% percentile (95% CI)	1.28 (0.92, 1.68)	2.69 (1.87, 3.25)
Median (95% CI)	NE (3.35, NE)	11.04 (7.03, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.2, 13.0*	0.1, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.662 (0.147)
95% CI		(0.496, 0.883)
Log-rank p-value		0.006

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
Serious TEAE
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	61.7 (54.5, 68.8)	72.0 (67.4, 76.6)
6 months	50.1 (38.4, 61.9)	58.3 (52.4, 64.1)
9 months	50.1 (38.4, 61.9)	50.0 (42.2, 57.9)
12 months	50.1 (38.4, 61.9)	40.4 (26.6, 54.3)
18 months	NE (NE, NE)	40.4 (26.6, 54.3)
Median Follow-up Time (months)	2.56	3.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE ≤ CTCAE Grade 2
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	36 (80.0)	71 (93.4)
Number of Subjects Censored, n (%)	9 (20.0)	5 (6.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.46)	0.13 (0.07, 0.26)
Median (95% CI)	0.66 (0.36, 0.69)	0.54 (0.26, 0.69)
75% percentile (95% CI)	1.61 (0.69, NE)	0.72 (0.69, 1.12)
Min, Max	0.0, 4.7*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.316 (0.215)
95% CI		(0.863, 2.006)
Log-rank p-value		0.240

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE ≤ CTCAE Grade 2
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	19.8 (8.0, 31.5)	7.3 (1.3, 13.3)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.66	0.54

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE ≤ CTCAE Grade 2
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	164 (88.6)	373 (98.2)
Number of Subjects Censored, n (%)	21 (11.4)	7 (1.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.10 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.49 (0.36, 0.69)	0.26 (0.23, 0.36)
75% percentile (95% CI)	0.76 (0.69, 1.02)	0.69 (NE, NE)
Min, Max	0.0, 3.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.453 (0.095)
95% CI		(1.205, 1.751)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE ≤ CTCAE Grade 2
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	9.0 (4.5, 13.5)	1.4 (0.1, 2.7)
6 months	NE (NE, NE)	0.5 (0.0, 1.3)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.49	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE ≥ CTCAE Grade 3
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	20 (44.4)	40 (52.6)
Number of Subjects Censored, n (%)	25 (55.6)	36 (47.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.62, 2.00)	1.40 (0.69, 1.87)
Median (95% CI)	4.83 (1.94, NE)	4.90 (2.20, 9.20)
75% percentile (95% CI)	NE (4.83, NE)	NE (7.10, NE)
Min, Max	0.1, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.100 (0.289)
95% CI		(0.624, 1.939)
Log-rank p-value		0.624

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE ≥ CTCAE Grade 3
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	59.6 (45.2, 74.1)	56.1 (44.9, 67.4)
6 months	NE (NE, NE)	41.2 (27.0, 55.3)
9 months	NE (NE, NE)	36.0 (20.5, 51.6)
12 months	NE (NE, NE)	28.8 (11.1, 46.6)
18 months	NE (NE, NE)	28.8 (11.1, 46.6)
Median Follow-up Time (months)	2.83	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE ≥ CTCAE Grade 3
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	96 (51.9)	246 (64.7)
Number of Subjects Censored, n (%)	89 (48.1)	134 (35.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.72, 1.25)	0.94 (0.69, 1.15)
Median (95% CI)	3.35 (2.00, 5.36)	2.76 (2.00, 3.25)
75% percentile (95% CI)	9.26 (5.36, NE)	8.38 (6.90, NE)
Min, Max	0.1, 9.3	0.0, 16.1
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.093 (0.122)
95% CI		(0.860, 1.389)
Log-rank p-value		0.344

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE ≥ CTCAE Grade 3
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	52.9 (45.6, 60.2)	46.9 (41.8, 52.0)
6 months	32.2 (19.4, 45.1)	32.9 (27.5, 38.3)
9 months	32.2 (19.4, 45.1)	22.3 (15.5, 29.2)
12 months	0.0 (NE, NE)	15.9 (6.6, 25.1)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.20	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
Discontinuation due to TEAE
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	4 (8.9)	14 (18.4)
Number of Subjects Censored, n (%)	41 (91.1)	62 (81.6)
Time to first TEAE (months)		
25% percentile (95% CI)	4.83 (3.65, NE)	NE (3.25, NE)
Median (95% CI)	4.83 (3.65, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (4.83, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.649 (0.601)
95% CI		(0.507, 5.358)
Log-rank p-value		0.315

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
Discontinuation due to TEAE
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (88.1, 100.0)	86.1 (78.1, 94.1)
6 months	NE (NE, NE)	75.3 (62.9, 87.7)
9 months	NE (NE, NE)	75.3 (62.9, 87.7)
12 months	NE (NE, NE)	75.3 (62.9, 87.7)
18 months	NE (NE, NE)	75.3 (62.9, 87.7)
Median Follow-up Time (months)	2.83	3.47

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
Discontinuation due to TEAE
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	45 (24.3)	79 (20.8)
Number of Subjects Censored, n (%)	140 (75.7)	301 (79.2)
Time to first TEAE (months)		
25% percentile (95% CI)	3.19 (1.54, NE)	7.46 (5.39, 8.38)
Median (95% CI)	NE (NE, NE)	NE (11.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.554 (0.195)
95% CI		(0.378, 0.813)
Log-rank p-value		0.004

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
Discontinuation due to TEAE
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.0 (72.0, 84.0)	86.6 (83.2, 90.1)
6 months	65.6 (54.0, 77.1)	79.3 (74.4, 84.1)
9 months	65.6 (54.0, 77.1)	65.5 (57.0, 74.0)
12 months	65.6 (54.0, 77.1)	59.2 (47.7, 70.6)
18 months	NE (NE, NE)	59.2 (47.7, 70.6)
Median Follow-up Time (months)	2.79	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
Deaths (Grade 5 TEAEs)
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	5 (11.1)	5 (6.6)
Number of Subjects Censored, n (%)	40 (88.9)	71 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.46, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 5.6*	0.8, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.675 (0.651)
95% CI		(0.188, 2.418)
Log-rank p-value		0.499

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
Deaths (Grade 5 TEAEs)
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.7 (77.6, 97.9)	93.4 (87.7, 99.0)
6 months	NE (NE, NE)	93.4 (87.7, 99.0)
9 months	NE (NE, NE)	93.4 (87.7, 99.0)
12 months	NE (NE, NE)	93.4 (87.7, 99.0)
18 months	NE (NE, NE)	93.4 (87.7, 99.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3J
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines
Safety Population
Deaths (Grade 5 TEAEs)
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	40 (21.6)	43 (11.3)
Number of Subjects Censored, n (%)	145 (78.4)	337 (88.7)
Time to first TEAE (months)		
25% percentile (95% CI)	3.75 (2.30, NE)	12.22 (8.87, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.6, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.329 (0.230)
95% CI		(0.209, 0.516)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE
<=3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.5 (72.3, 84.7)	93.9 (91.5, 96.4)
6 months	71.9 (62.6, 81.1)	86.3 (81.9, 90.7)
9 months	71.9 (62.6, 81.1)	81.2 (74.5, 88.0)
12 months	71.9 (62.6, 81.1)	78.2 (69.5, 86.9)
18 months	NE (NE, NE)	70.4 (53.9, 86.9)
Median Follow-up Time (months)	2.83	4.01

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	55 (85.9)	121 (97.6)
Number of Subjects Censored, n (%)	9 (14.1)	3 (2.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.21 (0.07, 0.36)	0.13 (0.07, 0.16)
Median (95% CI)	0.67 (0.46, 0.69)	0.38 (0.26, 0.46)
75% percentile (95% CI)	1.31 (0.69, 3.65)	0.69 (0.66, 0.72)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.641 (0.169)
95% CI		(1.179, 2.285)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	15.6 (6.7, 24.5)	3.2 (0.1, 6.3)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.67	0.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	158 (95.2)	330 (99.4)
Number of Subjects Censored, n (%)	8 (4.8)	2 (0.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.16)	0.07 (NE, NE)
Median (95% CI)	0.44 (0.30, 0.53)	0.23 (0.16, 0.30)
75% percentile (95% CI)	0.69 (0.69, 0.72)	0.69 (0.59, 0.69)
Min, Max	0.0, 3.2*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.317 (0.098)
95% CI		(1.087, 1.597)
Log-rank p-value		0.006

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	4.6 (1.4, 7.9)	1.2 (0.0, 2.4)
6 months	NE (NE, NE)	0.4 (0.0, 1.2)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.44	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Serious TEAE
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	22 (34.4)	46 (37.1)
Number of Subjects Censored, n (%)	42 (65.6)	78 (62.9)
Time to first TEAE (months)		
25% percentile (95% CI)	2.00 (1.02, 3.65)	2.40 (1.58, 3.98)
Median (95% CI)	NE (3.19, NE)	NE (5.32, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.813 (0.270)
95% CI		(0.478, 1.381)
Log-rank p-value		0.572

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Serious TEAE
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	67.7 (56.0, 79.4)	71.5 (63.5, 79.5)
6 months	NE (NE, NE)	60.4 (50.5, 70.3)
9 months	NE (NE, NE)	54.9 (43.4, 66.5)
12 months	NE (NE, NE)	51.3 (38.4, 64.1)
18 months	NE (NE, NE)	51.3 (38.4, 64.1)
Median Follow-up Time (months)	2.83	3.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Serious TEAE
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	66 (39.8)	125 (37.7)
Number of Subjects Censored, n (%)	100 (60.2)	207 (62.3)
Time to first TEAE (months)		
25% percentile (95% CI)	1.22 (0.79, 1.58)	2.83 (1.87, 3.29)
Median (95% CI)	NE (3.35, NE)	8.90 (6.90, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (11.96, NE)
Min, Max	0.2, 13.0*	0.1, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.658 (0.156)
95% CI		(0.484, 0.893)
Log-rank p-value		0.010

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Serious TEAE
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	61.8 (54.3, 69.3)	72.5 (67.6, 77.5)
6 months	51.4 (39.4, 63.4)	58.5 (52.1, 64.8)
9 months	51.4 (39.4, 63.4)	48.5 (39.6, 57.4)
12 months	51.4 (39.4, 63.4)	37.4 (22.1, 52.8)
18 months	NE (NE, NE)	37.4 (22.1, 52.8)
Median Follow-up Time (months)	2.58	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE ≤ CTCAE Grade 2
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	52 (81.3)	118 (95.2)
Number of Subjects Censored, n (%)	12 (18.8)	6 (4.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.21 (0.07, 0.46)	0.13 (0.07, 0.23)
Median (95% CI)	0.69 (0.46, 0.69)	0.46 (0.33, 0.66)
75% percentile (95% CI)	1.48 (0.69, NE)	0.71 (0.69, 0.85)
Min, Max	0.0, 4.7*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.507 (0.171)
95% CI		(1.078, 2.108)
Log-rank p-value		0.034

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE ≤ CTCAE Grade 2
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	18.6 (9.0, 28.2)	4.4 (0.5, 8.2)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.69	0.46

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE ≤ CTCAE Grade 2
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	148 (89.2)	326 (98.2)
Number of Subjects Censored, n (%)	18 (10.8)	6 (1.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.16)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.33, 0.62)	0.26 (0.20, 0.33)
75% percentile (95% CI)	0.72 (0.69, 1.02)	0.69 (0.66, 0.69)
Min, Max	0.0, 3.2*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.413 (0.101)
95% CI		(1.160, 1.721)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE ≤ CTCAE Grade 2
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	8.1 (3.5, 12.7)	1.7 (0.2, 3.2)
6 months	NE (NE, NE)	0.6 (0.0, 1.6)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE ≥ CTCAE Grade 3
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	29 (45.3)	73 (58.9)
Number of Subjects Censored, n (%)	35 (54.7)	51 (41.1)
Time to first TEAE (months)		
25% percentile (95% CI)	1.30 (0.72, 2.00)	1.23 (0.69, 1.61)
Median (95% CI)	3.65 (2.00, NE)	3.58 (2.23, 5.19)
75% percentile (95% CI)	4.83 (4.83, NE)	9.20 (7.10, NE)
Min, Max	0.1, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.119 (0.228)
95% CI		(0.716, 1.748)
Log-rank p-value		0.525

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE ≥ CTCAE Grade 3
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	58.6 (46.4, 70.9)	54.5 (45.7, 63.3)
6 months	NE (NE, NE)	35.8 (25.4, 46.1)
9 months	NE (NE, NE)	26.5 (14.6, 38.4)
12 months	NE (NE, NE)	22.1 (9.4, 34.7)
18 months	NE (NE, NE)	22.1 (9.4, 34.7)
Median Follow-up Time (months)	2.81	2.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE ≥ CTCAE Grade 3
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	87 (52.4)	213 (64.2)
Number of Subjects Censored, n (%)	79 (47.6)	119 (35.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.92 (0.69, 1.22)	0.92 (0.69, 1.15)
Median (95% CI)	3.35 (1.87, 5.36)	2.69 (1.97, 3.25)
75% percentile (95% CI)	9.26 (5.55, NE)	8.90 (6.90, NE)
Min, Max	0.1, 9.3	0.0, 16.1
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.082 (0.129)
95% CI		(0.840, 1.394)
Log-rank p-value		0.427

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE ≥ CTCAE Grade 3
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	52.5 (44.8, 60.2)	46.1 (40.7, 51.6)
6 months	32.7 (19.7, 45.8)	33.6 (27.8, 39.4)
9 months	32.7 (19.7, 45.8)	24.2 (16.9, 31.4)
12 months	0.0 (NE, NE)	16.9 (6.9, 26.9)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.12	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Discontinuation due to TEAE
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	8 (12.5)	24 (19.4)
Number of Subjects Censored, n (%)	56 (87.5)	100 (80.6)
Time to first TEAE (months)		
25% percentile (95% CI)	4.83 (3.19, NE)	8.28 (3.52, NE)
Median (95% CI)	4.83 (3.65, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (4.83, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.019 (0.430)
95% CI		(0.438, 2.366)
Log-rank p-value		0.916

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Discontinuation due to TEAE
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (83.9, 98.6)	85.8 (79.5, 92.0)
6 months	NE (NE, NE)	77.8 (69.0, 86.7)
9 months	NE (NE, NE)	70.7 (58.3, 83.1)
12 months	NE (NE, NE)	70.7 (58.3, 83.1)
18 months	NE (NE, NE)	70.7 (58.3, 83.1)
Median Follow-up Time (months)	2.83	3.56

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Discontinuation due to TEAE
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	41 (24.7)	69 (20.8)
Number of Subjects Censored, n (%)	125 (75.3)	263 (79.2)
Time to first TEAE (months)		
25% percentile (95% CI)	3.98 (1.28, NE)	7.03 (5.26, 8.90)
Median (95% CI)	NE (NE, NE)	NE (11.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.557 (0.206)
95% CI		(0.373, 0.834)
Log-rank p-value		0.006

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Discontinuation due to TEAE
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.4 (71.0, 83.8)	86.8 (83.2, 90.5)
6 months	66.5 (55.0, 78.1)	79.0 (73.7, 84.2)
9 months	66.5 (55.0, 78.1)	66.5 (57.7, 75.2)
12 months	66.5 (55.0, 78.1)	59.2 (46.8, 71.6)
18 months	NE (NE, NE)	59.2 (46.8, 71.6)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Deaths (Grade 5 TEAEs)
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	11 (17.2)	9 (7.3)
Number of Subjects Censored, n (%)	53 (82.8)	115 (92.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.30, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 5.6*	0.8, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.281 (0.484)
95% CI		(0.109, 0.725)
Log-rank p-value		0.007

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Deaths (Grade 5 TEAEs)
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.6 (72.7, 92.5)	95.1 (91.3, 98.9)
6 months	NE (NE, NE)	90.1 (83.5, 96.8)
9 months	NE (NE, NE)	90.1 (83.5, 96.8)
12 months	NE (NE, NE)	90.1 (83.5, 96.8)
18 months	NE (NE, NE)	90.1 (83.5, 96.8)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3K
Summary of Time to Onset of Overall TEAE by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Deaths (Grade 5 TEAEs)
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	34 (20.5)	39 (11.7)
Number of Subjects Censored, n (%)	132 (79.5)	293 (88.3)
Time to first TEAE (months)		
25% percentile (95% CI)	3.98 (2.37, NE)	12.22 (8.87, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.6, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.371 (0.245)
95% CI		(0.230, 0.600)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.5 (73.1, 85.9)	93.3 (90.6, 96.1)
6 months	74.3 (65.1, 83.5)	86.4 (81.7, 91.0)
9 months	74.3 (65.1, 83.5)	80.5 (72.9, 88.0)
12 months	74.3 (65.1, 83.5)	77.0 (67.1, 86.8)
18 months	NE (NE, NE)	68.4 (50.4, 86.5)
Median Follow-up Time (months)	2.83	4.07

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	204 (92.3)	436 (99.1)
Number of Subjects Censored, n (%)	17 (7.7)	4 (0.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.10 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.39, 0.59)	0.26 (0.23, 0.33)
75% percentile (95% CI)	0.72 (0.69, 0.82)	0.69 (0.66, 0.69)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.442 (0.086)
95% CI		(1.217, 1.708)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	7.6 (4.1, 11.1)	1.4 (0.3, 2.4)
6 months	NE (NE, NE)	0.7 (0.0, 1.5)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
TEAE
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	9 (100.0)	15 (93.8)
Number of Subjects Censored, n (%)	0	1 (6.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.23 (0.03, 0.33)	0.07 (0.03, 0.07)
Median (95% CI)	0.33 (0.03, 1.35)	0.11 (0.07, 0.62)
75% percentile (95% CI)	0.69 (0.30, NE)	0.66 (0.07, NE)
Min, Max	0.0, 3.6	0.0, 3.5
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.217 (0.856)
95% CI		(0.227, 6.513)
Log-rank p-value		0.647

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
TEAE
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	11.1 (0.0, 31.6)	12.5 (0.0, 28.7)
6 months	0.0 (NE, NE)	0.0 (NE, NE)
9 months	0.0 (NE, NE)	0.0 (NE, NE)
12 months	0.0 (NE, NE)	0.0 (NE, NE)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.33	0.11

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
Serious TEAE
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	83 (37.6)	165 (37.5)
Number of Subjects Censored, n (%)	138 (62.4)	275 (62.5)
Time to first TEAE (months)		
25% percentile (95% CI)	1.31 (0.99, 2.00)	2.69 (1.87, 3.22)
Median (95% CI)	NE (4.14, NE)	8.90 (7.75, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.724 (0.138)
95% CI		(0.552, 0.949)
Log-rank p-value		0.025

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
Serious TEAE
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	63.9 (57.4, 70.3)	71.7 (67.4, 76.0)
6 months	53.9 (43.2, 64.6)	58.9 (53.4, 64.3)
9 months	53.9 (43.2, 64.6)	49.7 (42.3, 57.0)
12 months	53.9 (43.2, 64.6)	42.3 (30.9, 53.8)
18 months	NE (NE, NE)	42.3 (30.9, 53.8)
Median Follow-up Time (months)	2.79	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
Serious TEAE
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	5 (55.6)	6 (37.5)
Number of Subjects Censored, n (%)	4 (44.4)	10 (62.5)
Time to first TEAE (months)		
25% percentile (95% CI)	1.81 (0.49, NE)	4.21 (1.51, NE)
Median (95% CI)	2.30 (0.49, NE)	NE (3.61, NE)
75% percentile (95% CI)	3.65 (2.30, NE)	NE (9.23, NE)
Min, Max	0.5, 3.6	1.5, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.039 (1.600)
95% CI		(0.002, 0.887)
Log-rank p-value		0.050

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
Serious TEAE
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	44.4 (3.4, 85.5)	87.1 (70.3, 100.0)
6 months	0.0 (NE, NE)	63.3 (37.4, 89.3)
9 months	0.0 (NE, NE)	63.3 (37.4, 89.3)
12 months	0.0 (NE, NE)	50.6 (20.3, 81.0)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.57

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
TEAE ≤ CTCAE Grade 2
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	192 (86.9)	429 (97.5)
Number of Subjects Censored, n (%)	29 (13.1)	11 (2.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.10 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.56 (0.46, 0.69)	0.30 (0.26, 0.39)
75% percentile (95% CI)	0.76 (0.69, 1.25)	0.69 (NE, NE)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.476 (0.088)
95% CI		(1.241, 1.755)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
TEAE ≤ CTCAE Grade 2
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	11.4 (6.9, 15.8)	2.0 (0.6, 3.4)
6 months	NE (NE, NE)	1.0 (0.0, 2.2)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.56	0.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
TEAE ≤ CTCAE Grade 2
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	8 (88.9)	15 (93.8)
Number of Subjects Censored, n (%)	1 (11.1)	1 (6.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.23 (0.03, 0.33)	0.07 (0.03, 0.07)
Median (95% CI)	0.33 (0.03, 1.35)	0.11 (0.07, 0.69)
75% percentile (95% CI)	0.69 (0.30, NE)	0.69 (0.07, NE)
Min, Max	0.0, 4.7*	0.0, 3.5
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.710 (0.808)
95% CI		(0.146, 3.461)
Log-rank p-value		0.701

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
TEAE ≤ CTCAE Grade 2
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	11.1 (0.0, 31.6)	12.5 (0.0, 28.7)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.33	0.11

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
TEAE ≥ CTCAE Grade 3
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	111 (50.2)	275 (62.5)
Number of Subjects Censored, n (%)	110 (49.8)	165 (37.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.72, 1.25)	0.95 (0.69, 1.18)
Median (95% CI)	3.61 (2.27, 5.36)	2.83 (2.43, 3.58)
75% percentile (95% CI)	9.26 (5.55, NE)	8.90 (7.33, NE)
Min, Max	0.1, 9.3	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.097 (0.114)
95% CI		(0.877, 1.373)
Log-rank p-value		0.334

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
TEAE ≥ CTCAE Grade 3
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	54.2 (47.6, 60.9)	48.3 (43.6, 53.1)
6 months	33.1 (20.6, 45.6)	34.3 (29.1, 39.5)
9 months	33.1 (20.6, 45.6)	24.0 (17.5, 30.5)
12 months	0.0 (NE, NE)	18.7 (10.3, 27.0)
18 months	0.0 (NE, NE)	12.4 (1.0, 23.9)
Median Follow-up Time (months)	2.37	2.64

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
TEAE ≥ CTCAE Grade 3
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	5 (55.6)	11 (68.8)
Number of Subjects Censored, n (%)	4 (44.4)	5 (31.3)
Time to first TEAE (months)		
25% percentile (95% CI)	1.81 (0.49, NE)	0.41 (0.07, 2.79)
Median (95% CI)	3.65 (0.49, NE)	3.20 (0.20, 9.20)
75% percentile (95% CI)	3.65 (1.87, NE)	9.20 (2.79, NE)
Min, Max	0.5, 3.6	0.1, 9.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.038 (0.858)
95% CI		(0.193, 5.576)
Log-rank p-value		0.763

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
TEAE ≥ CTCAE Grade 3
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	55.6 (23.1, 88.0)	50.0 (25.5, 74.5)
6 months	0.0 (NE, NE)	33.3 (8.4, 58.3)
9 months	0.0 (NE, NE)	33.3 (8.4, 58.3)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
Discontinuation due to TEAE
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	45 (20.4)	89 (20.2)
Number of Subjects Censored, n (%)	176 (79.6)	351 (79.8)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (3.15, NE)	7.03 (5.39, 8.90)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.669 (0.191)
95% CI		(0.460, 0.972)
Log-rank p-value		0.042

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
Discontinuation due to TEAE
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.0 (76.9, 87.1)	86.5 (83.3, 89.8)
6 months	67.1 (54.7, 79.5)	78.7 (74.1, 83.3)
9 months	67.1 (54.7, 79.5)	67.6 (60.1, 75.1)
12 months	67.1 (54.7, 79.5)	62.4 (52.5, 72.3)
18 months	NE (NE, NE)	62.4 (52.5, 72.3)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
Discontinuation due to TEAE
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	4 (44.4)	4 (25.0)
Number of Subjects Censored, n (%)	5 (55.6)	12 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.79 (1.35, NE)	7.52 (1.51, NE)
Median (95% CI)	3.65 (1.35, NE)	NE (4.37, NE)
75% percentile (95% CI)	3.65 (1.81, NE)	NE (NE, NE)
Min, Max	1.2*, 3.6	1.5, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.012 (1.876)
95% CI		(0.000, 0.478)
Log-rank p-value		0.050

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
Discontinuation due to TEAE
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	62.5 (29.0, 96.0)	87.1 (70.3, 100.0)
6 months	0.0 (NE, NE)	78.3 (56.2, 100.0)
9 months	0.0 (NE, NE)	67.2 (39.4, 94.9)
12 months	0.0 (NE, NE)	67.2 (39.4, 94.9)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	5.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
Deaths (Grade 5 TEAEs)
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	43 (19.5)	47 (10.7)
Number of Subjects Censored, n (%)	178 (80.5)	393 (89.3)
Time to first TEAE (months)		
25% percentile (95% CI)	3.98 (2.76, NE)	12.22 (9.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.356 (0.221)
95% CI		(0.231, 0.549)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
Deaths (Grade 5 TEAEs)
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.6 (75.1, 86.0)	93.6 (91.3, 95.9)
6 months	74.9 (66.7, 83.0)	87.2 (83.3, 91.2)
9 months	74.9 (66.7, 83.0)	82.8 (76.8, 88.8)
12 months	74.9 (66.7, 83.0)	80.3 (72.9, 87.8)
18 months	NE (NE, NE)	74.2 (60.6, 87.7)
Median Follow-up Time (months)	2.83	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3L
Summary of Time to Onset of Overall TEAE by Prior VEGFi
Safety Population
Deaths (Grade 5 TEAEs)
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	2 (22.2)	1 (6.3)
Number of Subjects Censored, n (%)	7 (77.8)	15 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	2.30 (1.22, NE)	NE (3.75, NE)
Median (95% CI)	NE (1.22, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (2.30, NE)	NE (NE, NE)
Min, Max	1.2, 4.7*	1.7*, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.000 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.1 (35.9, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	90.9 (73.9, 100.0)
9 months	NE (NE, NE)	90.9 (73.9, 100.0)
12 months	NE (NE, NE)	90.9 (73.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	5.04

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	84 (95.5)	177 (98.9)
Number of Subjects Censored, n (%)	4 (4.5)	2 (1.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.13)	0.07 (NE, NE)
Median (95% CI)	0.41 (0.23, 0.53)	0.23 (0.16, 0.30)
75% percentile (95% CI)	0.69 (0.66, 0.76)	0.69 (0.59, 0.69)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Min, Max	0.0, 3.6	0.0, 5.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.228 (0.135)
95% CI		(0.942, 1.600)
Log-rank p-value		0.148

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	5.7 (0.8, 10.5)	2.2 (0.1, 4.4)
6 months	0.0 (NE, NE)	0.0 (NE, NE)
9 months	0.0 (NE, NE)	0.0 (NE, NE)
12 months	0.0 (NE, NE)	0.0 (NE, NE)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.41	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
TEAE
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	129 (90.8)	274 (98.9)
Number of Subjects Censored, n (%)	13 (9.2)	3 (1.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.16 (0.07, 0.23)	0.10 (0.07, 0.10)
Median (95% CI)	0.56 (0.39, 0.69)	0.26 (0.23, 0.39)
75% percentile (95% CI)	0.72 (0.69, 1.15)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.542 (0.109)
95% CI		(1.244, 1.910)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
TEAE
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	9.0 (4.2, 13.7)	1.4 (0.0, 2.8)
6 months	NE (NE, NE)	1.0 (0.0, 2.2)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.56	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
Serious TEAE
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	31 (35.2)	69 (38.5)
Number of Subjects Censored, n (%)	57 (64.8)	110 (61.5)
Time to first TEAE (months)		
25% percentile (95% CI)	2.00 (0.95, 3.19)	2.76 (1.71, 3.61)
Median (95% CI)	4.14 (3.35, NE)	9.23 (7.03, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (11.04, NE)
Min, Max	0.2, 6.8*	0.1, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.731 (0.226)
95% CI		(0.469, 1.138)
Log-rank p-value		0.255

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
Serious TEAE
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	69.7 (59.9, 79.5)	72.0 (65.3, 78.7)
6 months	49.8 (32.5, 67.1)	59.4 (51.2, 67.6)
9 months	NE (NE, NE)	53.0 (42.9, 63.1)
12 months	NE (NE, NE)	30.1 (8.4, 51.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.52

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
Serious TEAE
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	57 (40.1)	102 (36.8)
Number of Subjects Censored, n (%)	85 (59.9)	175 (63.2)
Time to first TEAE (months)		
25% percentile (95% CI)	1.22 (0.76, 1.64)	2.73 (1.84, 3.32)
Median (95% CI)	NE (5.36, NE)	8.90 (6.90, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.649 (0.170)
95% CI		(0.465, 0.905)
Log-rank p-value		0.013

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
Serious TEAE
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	59.4 (51.2, 67.7)	72.4 (67.0, 77.8)
6 months	52.8 (38.6, 67.1)	58.7 (51.7, 65.7)
9 months	52.8 (38.6, 67.1)	49.2 (39.9, 58.5)
12 months	52.8 (38.6, 67.1)	49.2 (39.9, 58.5)
18 months	NE (NE, NE)	49.2 (39.9, 58.5)
Median Follow-up Time (months)	2.40	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
TEAE ≤ CTCAE Grade 2
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	78 (88.6)	177 (98.9)
Number of Subjects Censored, n (%)	10 (11.4)	2 (1.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.13)	0.07 (NE, NE)
Median (95% CI)	0.46 (0.23, 0.66)	0.23 (0.16, 0.36)
75% percentile (95% CI)	0.72 (0.69, 1.25)	0.69 (0.62, 0.69)
Min, Max	0.0, 4.7*	0.0, 5.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.390 (0.138)
95% CI		(1.061, 1.821)
Log-rank p-value		0.021

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
TEAE ≤ CTCAE Grade 2
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	10.4 (3.7, 17.0)	2.2 (0.1, 4.4)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.46	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
TEAE ≤ CTCAE Grade 2
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	122 (85.9)	267 (96.4)
Number of Subjects Censored, n (%)	20 (14.1)	10 (3.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.16 (0.07, 0.26)	0.10 (0.07, 0.13)
Median (95% CI)	0.59 (0.46, 0.69)	0.36 (0.26, 0.46)
75% percentile (95% CI)	0.92 (0.69, 1.61)	0.69 (0.69, 0.72)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.470 (0.112)
95% CI		(1.182, 1.830)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
TEAE ≤ CTCAE Grade 2
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	12.2 (6.5, 17.9)	2.5 (0.4, 4.6)
6 months	NE (NE, NE)	1.7 (0.0, 3.6)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.59	0.36

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
TEAE ≥ CTCAE Grade 3
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	45 (51.1)	116 (64.8)
Number of Subjects Censored, n (%)	43 (48.9)	63 (35.2)
Time to first TEAE (months)		
25% percentile (95% CI)	1.12 (0.72, 1.87)	0.99 (0.69, 1.35)
Median (95% CI)	3.35 (2.00, 4.83)	3.02 (2.27, 3.98)
75% percentile (95% CI)	NE (4.14, NE)	7.39 (5.95, NE)
Min, Max	0.1, 6.8*	0.1, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.060 (0.181)
95% CI		(0.744, 1.512)
Log-rank p-value		0.679

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
TEAE ≥ CTCAE Grade 3
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	56.3 (45.8, 66.8)	50.3 (42.9, 57.7)
6 months	31.9 (15.9, 47.8)	31.4 (23.2, 39.5)
9 months	NE (NE, NE)	24.8 (16.1, 33.5)
12 months	NE (NE, NE)	7.7 (0.0, 20.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.50	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
TEAE ≥ CTCAE Grade 3
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	71 (50.0)	170 (61.4)
Number of Subjects Censored, n (%)	71 (50.0)	107 (38.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.69, 1.22)	0.92 (0.69, 1.25)
Median (95% CI)	4.34 (1.94, NE)	2.79 (1.87, 3.84)
75% percentile (95% CI)	9.26 (5.36, NE)	8.90 (7.46, NE)
Min, Max	0.1, 9.3	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.105 (0.143)
95% CI		(0.834, 1.463)
Log-rank p-value		0.375

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
TEAE ≥ CTCAE Grade 3
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	52.8 (44.5, 61.2)	47.2 (41.2, 53.2)
6 months	31.1 (12.1, 50.2)	36.3 (29.9, 42.8)
9 months	31.1 (12.1, 50.2)	25.0 (16.6, 33.4)
12 months	0.0 (NE, NE)	25.0 (16.6, 33.4)
18 months	0.0 (NE, NE)	16.7 (2.2, 31.1)
Median Follow-up Time (months)	2.25	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
Discontinuation due to TEAE
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	20 (22.7)	35 (19.6)
Number of Subjects Censored, n (%)	68 (77.3)	144 (80.4)
Time to first TEAE (months)		
25% percentile (95% CI)	3.65 (2.10, 4.83)	7.52 (5.03, NE)
Median (95% CI)	NE (3.98, NE)	NE (11.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.565 (0.296)
95% CI		(0.317, 1.009)
Log-rank p-value		0.078

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
Discontinuation due to TEAE
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.8 (76.1, 91.6)	86.2 (81.1, 91.4)
6 months	51.6 (29.0, 74.1)	79.2 (72.2, 86.2)
9 months	NE (NE, NE)	74.9 (66.1, 83.7)
12 months	NE (NE, NE)	62.6 (45.2, 80.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
Discontinuation due to TEAE
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	29 (20.4)	58 (20.9)
Number of Subjects Censored, n (%)	113 (79.6)	219 (79.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.54, NE)	6.60 (4.76, 8.38)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.667 (0.238)
95% CI		(0.419, 1.063)
Log-rank p-value		0.081

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
Discontinuation due to TEAE
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.8 (73.0, 86.5)	86.8 (82.7, 90.8)
6 months	75.3 (64.8, 85.9)	78.3 (72.3, 84.2)
9 months	75.3 (64.8, 85.9)	62.8 (52.6, 72.9)
12 months	75.3 (64.8, 85.9)	62.8 (52.6, 72.9)
18 months	NE (NE, NE)	62.8 (52.6, 72.9)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
Deaths (Grade 5 TEAEs)
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	19 (21.6)	16 (8.9)
Number of Subjects Censored, n (%)	69 (78.4)	163 (91.1)
Time to first TEAE (months)		
25% percentile (95% CI)	3.75 (2.40, NE)	NE (9.69, NE)
Median (95% CI)	NE (3.98, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.9, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.262 (0.359)
95% CI		(0.130, 0.530)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
Deaths (Grade 5 TEAEs)
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.6 (71.9, 89.2)	94.1 (90.6, 97.7)
6 months	67.3 (51.4, 83.2)	89.0 (83.4, 94.5)
9 months	NE (NE, NE)	89.0 (83.4, 94.5)
12 months	NE (NE, NE)	82.6 (69.6, 95.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3M
Summary of Time to Onset of Overall TEAE by Prior EGFRi
Safety Population
Deaths (Grade 5 TEAEs)
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	26 (18.3)	32 (11.6)
Number of Subjects Censored, n (%)	116 (81.7)	245 (88.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.30, NE)	12.22 (8.21, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.391 (0.278)
95% CI		(0.227, 0.674)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE
TAS-102

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.2 (73.3, 87.1)	93.7 (90.8, 96.6)
6 months	80.2 (73.3, 87.1)	86.3 (81.0, 91.6)
9 months	80.2 (73.3, 87.1)	79.6 (71.3, 87.9)
12 months	80.2 (73.3, 87.1)	79.6 (71.3, 87.9)
18 months	NE (NE, NE)	69.7 (50.0, 89.3)
Median Follow-up Time (months)	2.83	3.78

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	109 (90.1)	234 (98.7)
Number of Subjects Censored, n (%)	12 (9.9)	3 (1.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.53 (0.36, 0.69)	0.26 (0.23, 0.39)
75% percentile (95% CI)	0.72 (0.69, 1.28)	0.69 (0.66, 0.69)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.435 (0.118)
95% CI		(1.138, 1.810)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	9.9 (4.6, 15.2)	2.1 (0.3, 3.9)
6 months	NE (NE, NE)	0.7 (0.0, 2.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.53	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	18 (100.0)	39 (97.5)
Number of Subjects Censored, n (%)	0	1 (2.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.30 (0.03, 0.66)	0.13 (0.07, 0.23)
Median (95% CI)	0.67 (0.30, 0.69)	0.39 (0.23, 0.46)
75% percentile (95% CI)	0.72 (0.69, 1.38)	0.69 (0.46, 0.69)
Min, Max	0.0, 3.6	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.461 (0.303)
95% CI		(0.806, 2.649)
Log-rank p-value		0.134

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	5.6 (0.0, 16.1)	2.5 (0.0, 7.3)
6 months	0.0 (NE, NE)	NE (NE, NE)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.67	0.39

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	86 (94.5)	178 (99.4)
Number of Subjects Censored, n (%)	5 (5.5)	1 (0.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.13 (0.03, 0.23)	0.07 (0.07, 0.10)
Median (95% CI)	0.39 (0.26, 0.49)	0.23 (0.16, 0.30)
75% percentile (95% CI)	0.69 (0.59, 0.92)	0.69 (0.56, 0.69)
Min, Max	0.0, 2.8*	0.0, 3.5
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.385 (0.134)
95% CI		(1.064, 1.802)
Log-rank p-value		0.013

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	NE (NE, NE)	1.1 (0.0, 2.7)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.39	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	49 (40.5)	84 (35.4)
Number of Subjects Censored, n (%)	72 (59.5)	153 (64.6)
Time to first TEAE (months)		
25% percentile (95% CI)	1.28 (0.99, 2.00)	2.83 (1.97, 3.48)
Median (95% CI)	NE (3.19, NE)	9.23 (7.79, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.604 (0.185)
95% CI		(0.420, 0.869)
Log-rank p-value		0.008

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	62.1 (53.4, 70.9)	73.5 (67.8, 79.2)
6 months	51.9 (39.5, 64.4)	63.3 (56.2, 70.4)
9 months	51.9 (39.5, 64.4)	51.4 (41.5, 61.4)
12 months	51.9 (39.5, 64.4)	42.6 (28.0, 57.2)
18 months	NE (NE, NE)	42.6 (28.0, 57.2)
Median Follow-up Time (months)	2.83	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	5 (27.8)	15 (37.5)
Number of Subjects Censored, n (%)	13 (72.2)	25 (62.5)
Time to first TEAE (months)		
25% percentile (95% CI)	3.65 (0.66, NE)	2.69 (0.95, 4.90)
Median (95% CI)	NE (3.65, NE)	NE (4.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	0.2, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.944 (0.529)
95% CI		(0.334, 2.661)
Log-rank p-value		0.913

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.8 (58.6, 97.0)	71.4 (57.0, 85.8)
6 months	62.2 (30.9, 93.5)	54.2 (35.6, 72.8)
9 months	NE (NE, NE)	54.2 (35.6, 72.8)
12 months	NE (NE, NE)	54.2 (35.6, 72.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	34 (37.4)	72 (40.2)
Number of Subjects Censored, n (%)	57 (62.6)	107 (59.8)
Time to first TEAE (months)		
25% percentile (95% CI)	1.31 (0.72, 2.30)	2.40 (1.61, 3.29)
Median (95% CI)	NE (5.36, NE)	11.96 (5.26, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (11.96, NE)
Min, Max	0.2, 8.4*	0.1, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.740 (0.215)
95% CI		(0.486, 1.126)
Log-rank p-value		0.160

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	62.0 (51.7, 72.4)	70.7 (63.9, 77.5)
6 months	51.7 (31.3, 72.1)	55.0 (46.3, 63.6)
9 months	NE (NE, NE)	51.1 (41.5, 60.8)
12 months	NE (NE, NE)	38.4 (15.5, 61.2)
18 months	NE (NE, NE)	38.4 (15.5, 61.2)
Median Follow-up Time (months)	2.40	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≤ CTCAE Grade 2
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	104 (86.0)	230 (97.0)
Number of Subjects Censored, n (%)	17 (14.0)	7 (3.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.59 (0.39, 0.69)	0.33 (0.23, 0.46)
75% percentile (95% CI)	0.76 (0.69, 1.87)	0.69 (0.69, 0.72)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.462 (0.120)
95% CI		(1.155, 1.851)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≤ CTCAE Grade 2
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	13.3 (7.1, 19.5)	3.1 (0.8, 5.4)
6 months	NE (NE, NE)	1.0 (0.0, 2.8)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.59	0.33

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≤ CTCAE Grade 2
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	17 (94.4)	39 (97.5)
Number of Subjects Censored, n (%)	1 (5.6)	1 (2.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.30 (0.03, 0.66)	0.13 (0.07, 0.26)
Median (95% CI)	0.67 (0.30, 0.69)	0.39 (0.23, 0.59)
75% percentile (95% CI)	0.72 (0.69, 1.38)	0.69 (0.46, 0.72)
Min, Max	0.0, 4.7*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.340 (0.305)
95% CI		(0.737, 2.435)
Log-rank p-value		0.240

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≤ CTCAE Grade 2
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	5.6 (0.0, 16.1)	2.5 (0.0, 7.3)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.67	0.39

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≤ CTCAE Grade 2
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	79 (86.8)	175 (97.8)
Number of Subjects Censored, n (%)	12 (13.2)	4 (2.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.13 (0.03, 0.23)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.26, 0.59)	0.26 (0.20, 0.36)
75% percentile (95% CI)	0.82 (0.69, 1.61)	0.69 (0.66, 0.69)
Min, Max	0.0, 2.8*	0.0, 3.5
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.471 (0.139)
95% CI		(1.120, 1.932)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≤ CTCAE Grade 2
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	NE (NE, NE)	1.5 (0.0, 3.5)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.46	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≥ CTCAE Grade 3
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	63 (52.1)	143 (60.3)
Number of Subjects Censored, n (%)	58 (47.9)	94 (39.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.02 (0.69, 1.28)	0.99 (0.72, 1.38)
Median (95% CI)	3.19 (1.94, 4.83)	3.12 (2.43, 4.57)
75% percentile (95% CI)	9.26 (4.83, NE)	9.20 (7.46, NE)
Min, Max	0.1, 9.3	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.963 (0.154)
95% CI		(0.712, 1.302)
Log-rank p-value		0.932

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≥ CTCAE Grade 3
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	53.2 (44.2, 62.2)	50.8 (44.4, 57.3)
6 months	34.2 (18.3, 50.1)	38.1 (30.9, 45.3)
9 months	34.2 (18.3, 50.1)	25.9 (17.1, 34.7)
12 months	0.0 (NE, NE)	19.5 (9.1, 29.9)
18 months	0.0 (NE, NE)	19.5 (9.1, 29.9)
Median Follow-up Time (months)	2.37	2.69

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≥ CTCAE Grade 3
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	6 (33.3)	28 (70.0)
Number of Subjects Censored, n (%)	12 (66.7)	12 (30.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.66, NE)	0.94 (0.39, 1.64)
Median (95% CI)	NE (1.87, NE)	2.53 (1.41, 4.90)
75% percentile (95% CI)	NE (3.65, NE)	5.19 (4.21, NE)
Min, Max	0.7, 6.5*	0.1, 7.3
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.607 (0.458)
95% CI		(1.063, 6.395)
Log-rank p-value		0.045

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≥ CTCAE Grade 3
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.2 (51.5, 92.9)	43.9 (28.2, 59.6)
6 months	57.8 (27.5, 88.0)	17.8 (1.5, 34.1)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.83	2.45

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≥ CTCAE Grade 3
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	47 (51.6)	115 (64.2)
Number of Subjects Censored, n (%)	44 (48.4)	64 (35.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.92 (0.69, 1.31)	0.85 (0.62, 1.18)
Median (95% CI)	3.61 (1.87, 5.55)	2.60 (1.71, 3.61)
75% percentile (95% CI)	5.55 (5.36, NE)	11.96 (6.05, NE)
Min, Max	0.1, 6.4*	0.1, 16.1
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.083 (0.178)
95% CI		(0.765, 1.535)
Log-rank p-value		0.662

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≥ CTCAE Grade 3
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	52.0 (41.5, 62.4)	46.2 (38.7, 53.6)
6 months	20.8 (0.0, 42.7)	32.8 (25.2, 40.5)
9 months	NE (NE, NE)	29.2 (20.8, 37.6)
12 months	NE (NE, NE)	19.5 (2.9, 36.1)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.04	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
Discontinuation due to TEAE
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	22 (18.2)	53 (22.4)
Number of Subjects Censored, n (%)	99 (81.8)	184 (77.6)
Time to first TEAE (months)		
25% percentile (95% CI)	4.57 (3.15, NE)	7.46 (4.27, 9.69)
Median (95% CI)	NE (4.83, NE)	NE (11.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.820 (0.264)
95% CI		(0.489, 1.376)
Log-rank p-value		0.502

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
Discontinuation due to TEAE
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.4 (79.0, 91.8)	84.9 (80.2, 89.5)
6 months	61.1 (39.8, 82.3)	78.9 (72.9, 84.8)
9 months	61.1 (39.8, 82.3)	66.3 (56.6, 76.0)
12 months	61.1 (39.8, 82.3)	57.4 (42.7, 72.1)
18 months	NE (NE, NE)	57.4 (42.7, 72.1)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
Discontinuation due to TEAE
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	5 (27.8)	5 (12.5)
Number of Subjects Censored, n (%)	13 (72.2)	35 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	3.65 (0.66, NE)	NE (4.90, NE)
Median (95% CI)	NE (3.65, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	0.5, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.346 (0.708)
95% CI		(0.086, 1.385)
Log-rank p-value		0.129

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
Discontinuation due to TEAE
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.8 (58.6, 97.0)	92.4 (84.0, 100.0)
6 months	64.8 (36.6, 93.0)	81.2 (64.9, 97.6)
9 months	NE (NE, NE)	81.2 (64.9, 97.6)
12 months	NE (NE, NE)	81.2 (64.9, 97.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
Discontinuation due to TEAE
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	22 (24.2)	35 (19.6)
Number of Subjects Censored, n (%)	69 (75.8)	144 (80.4)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (0.76, NE)	6.90 (4.76, NE)
Median (95% CI)	NE (4.34, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.491 (0.293)
95% CI		(0.277, 0.871)
Log-rank p-value		0.014

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
Discontinuation due to TEAE
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.5 (67.7, 85.3)	87.5 (82.6, 92.4)
6 months	68.8 (52.6, 85.1)	78.0 (70.6, 85.4)
9 months	NE (NE, NE)	66.7 (54.5, 79.0)
12 months	NE (NE, NE)	66.7 (54.5, 79.0)
18 months	NE (NE, NE)	66.7 (54.5, 79.0)
Median Follow-up Time (months)	2.79	4.07

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
Deaths (Grade 5 TEAEs)
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	25 (20.7)	18 (7.6)
Number of Subjects Censored, n (%)	96 (79.3)	219 (92.4)
Time to first TEAE (months)		
25% percentile (95% CI)	3.98 (2.40, NE)	NE (9.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.8, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.243 (0.324)
95% CI		(0.128, 0.458)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
Deaths (Grade 5 TEAEs)
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.4 (71.9, 87.0)	95.1 (92.3, 97.9)
6 months	72.7 (61.0, 84.5)	91.6 (87.2, 95.9)
9 months	72.7 (61.0, 84.5)	87.4 (80.0, 94.8)
12 months	72.7 (61.0, 84.5)	83.6 (73.4, 93.7)
18 months	NE (NE, NE)	83.6 (73.4, 93.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
Deaths (Grade 5 TEAEs)
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	6 (15.0)
Number of Subjects Censored, n (%)	17 (94.4)	34 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.77, NE)	NE (3.22, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8, 6.5*	1.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.934 (1.101)
95% CI		(0.224, 16.731)
Log-rank p-value		0.519

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
Deaths (Grade 5 TEAEs)
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (83.9, 100.0)	89.8 (80.3, 99.3)
6 months	94.4 (83.9, 100.0)	86.3 (75.1, 97.6)
9 months	NE (NE, NE)	80.2 (64.5, 95.8)
12 months	NE (NE, NE)	80.2 (64.5, 95.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3N
Summary of Time to Onset of Overall TEAE by Prior TAS-102 and/or Regorafenib
Safety Population
Deaths (Grade 5 TEAEs)
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	19 (20.9)	24 (13.4)
Number of Subjects Censored, n (%)	72 (79.1)	155 (86.6)
Time to first TEAE (months)		
25% percentile (95% CI)	3.75 (1.68, NE)	12.22 (5.95, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 8.4*	0.6, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.361 (0.327)
95% CI		(0.191, 0.685)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.7 (69.9, 87.6)	93.1 (89.3, 96.9)
6 months	73.1 (59.7, 86.5)	82.4 (75.1, 89.7)
9 months	NE (NE, NE)	78.6 (68.7, 88.6)
12 months	NE (NE, NE)	78.6 (68.7, 88.6)
18 months	NE (NE, NE)	65.5 (40.7, 90.4)
Median Follow-up Time (months)	2.79	4.37

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	145 (93.5)	331 (98.8)
Number of Subjects Censored, n (%)	10 (6.5)	4 (1.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.10 (0.07, 0.23)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.36, 0.59)	0.26 (0.23, 0.33)
75% percentile (95% CI)	0.69 (0.69, 0.72)	0.69 (0.66, 0.69)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.329 (0.102)
95% CI		(1.089, 1.621)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	6.3 (2.4, 10.1)	1.8 (0.4, 3.2)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
TEAE
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	68 (90.7)	120 (99.2)
Number of Subjects Censored, n (%)	7 (9.3)	1 (0.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.59 (0.26, 0.69)	0.26 (0.20, 0.39)
75% percentile (95% CI)	1.02 (0.72, 1.87)	0.69 (0.59, 0.69)
Min, Max	0.0, 3.6	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.632 (0.161)
95% CI		(1.191, 2.236)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
TEAE
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	10.7 (3.7, 17.7)	1.7 (0.0, 3.9)
6 months	0.0 (NE, NE)	0.8 (0.0, 2.4)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.59	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
Serious TEAE
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	63 (40.6)	125 (37.3)
Number of Subjects Censored, n (%)	92 (59.4)	210 (62.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.02 (0.76, 1.64)	2.53 (1.71, 3.25)
Median (95% CI)	NE (3.15, NE)	8.28 (6.90, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (11.04, NE)
Min, Max	0.2, 6.5*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.598 (0.162)
95% CI		(0.436, 0.821)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
Serious TEAE
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	59.4 (51.5, 67.3)	71.7 (66.7, 76.6)
6 months	54.6 (44.8, 64.3)	57.2 (50.6, 63.8)
9 months	NE (NE, NE)	47.1 (37.8, 56.5)
12 months	NE (NE, NE)	38.0 (23.6, 52.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.40	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
Serious TEAE
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	25 (33.3)	46 (38.0)
Number of Subjects Censored, n (%)	50 (66.7)	75 (62.0)
Time to first TEAE (months)		
25% percentile (95% CI)	2.00 (1.25, 4.14)	2.86 (1.81, 4.21)
Median (95% CI)	NE (4.14, NE)	11.96 (7.03, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.792 (0.256)
95% CI		(0.479, 1.308)
Log-rank p-value		0.533

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
Serious TEAE
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.4 (61.1, 81.8)	73.8 (65.9, 81.8)
6 months	54.7 (37.0, 72.3)	62.9 (53.6, 72.1)
9 months	54.7 (37.0, 72.3)	56.6 (45.9, 67.4)
12 months	54.7 (37.0, 72.3)	49.6 (33.5, 65.6)
18 months	NE (NE, NE)	49.6 (33.5, 65.6)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
TEAE ≤ CTCAE Grade 2
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	134 (86.5)	324 (96.7)
Number of Subjects Censored, n (%)	21 (13.5)	11 (3.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.10 (0.07, 0.23)	0.07 (0.07, 0.10)
Median (95% CI)	0.53 (0.39, 0.66)	0.30 (0.23, 0.46)
75% percentile (95% CI)	0.72 (0.69, 1.02)	0.69 (NE, NE)
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.381 (0.104)
95% CI		(1.126, 1.695)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
TEAE ≤ CTCAE Grade 2
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	11.0 (5.6, 16.5)	2.7 (0.8, 4.6)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.53	0.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
TEAE ≤ CTCAE Grade 2
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	66 (88.0)	120 (99.2)
Number of Subjects Censored, n (%)	9 (12.0)	1 (0.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.59 (0.30, 0.69)	0.26 (0.23, 0.39)
75% percentile (95% CI)	1.02 (0.72, 1.87)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.639 (0.162)
95% CI		(1.193, 2.252)
Log-rank p-value		0.004

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
TEAE ≤ CTCAE Grade 2
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	12.0 (4.6, 19.4)	1.7 (0.0, 3.9)
6 months	NE (NE, NE)	0.8 (0.0, 2.4)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.59	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
TEAE ≥ CTCAE Grade 3
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	83 (53.5)	213 (63.6)
Number of Subjects Censored, n (%)	72 (46.5)	122 (36.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.72 (0.69, 0.99)	0.85 (0.69, 1.15)
Median (95% CI)	2.33 (1.87, 4.34)	2.76 (2.00, 3.35)
75% percentile (95% CI)	NE (4.34, NE)	7.62 (6.05, NE)
Min, Max	0.1, 6.5*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.005 (0.133)
95% CI		(0.775, 1.303)
Log-rank p-value		0.980

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
TEAE ≥ CTCAE Grade 3
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	48.3 (40.3, 56.3)	47.3 (41.9, 52.8)
6 months	36.7 (24.3, 49.0)	31.1 (25.0, 37.2)
9 months	NE (NE, NE)	20.1 (12.0, 28.2)
12 months	NE (NE, NE)	11.7 (0.8, 22.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
TEAE ≥ CTCAE Grade 3
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	33 (44.0)	73 (60.3)
Number of Subjects Censored, n (%)	42 (56.0)	48 (39.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.38 (0.95, 3.35)	1.28 (0.69, 1.61)
Median (95% CI)	4.83 (3.35, NE)	3.61 (2.04, 6.67)
75% percentile (95% CI)	9.26 (5.36, NE)	16.07 (7.46, NE)
Min, Max	0.1, 9.3	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.140 (0.216)
95% CI		(0.747, 1.739)
Log-rank p-value		0.291

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
TEAE ≥ CTCAE Grade 3
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	66.2 (55.4, 77.0)	51.4 (42.4, 60.4)
6 months	33.4 (13.6, 53.2)	41.2 (31.8, 50.7)
9 months	33.4 (13.6, 53.2)	33.1 (22.6, 43.6)
12 months	0.0 (NE, NE)	27.6 (14.4, 40.7)
18 months	0.0 (NE, NE)	18.4 (1.2, 35.5)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
Discontinuation due to TEAE
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	38 (24.5)	71 (21.2)
Number of Subjects Censored, n (%)	117 (75.5)	264 (78.8)
Time to first TEAE (months)		
25% percentile (95% CI)	3.15 (1.28, NE)	6.90 (5.03, 8.90)
Median (95% CI)	NE (4.34, NE)	NE (11.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.545 (0.213)
95% CI		(0.359, 0.828)
Log-rank p-value		0.004

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
Discontinuation due to TEAE
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.8 (70.1, 83.6)	85.7 (81.9, 89.5)
6 months	64.6 (49.5, 79.7)	77.3 (71.8, 82.8)
9 months	NE (NE, NE)	65.0 (55.4, 74.5)
12 months	NE (NE, NE)	56.7 (42.9, 70.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
Discontinuation due to TEAE
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	11 (14.7)	22 (18.2)
Number of Subjects Censored, n (%)	64 (85.3)	99 (81.8)
Time to first TEAE (months)		
25% percentile (95% CI)	4.83 (3.65, NE)	8.21 (4.76, NE)
Median (95% CI)	NE (4.83, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.763 (0.392)
95% CI		(0.354, 1.644)
Log-rank p-value		0.733

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
Discontinuation due to TEAE
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.4 (83.6, 97.2)	88.9 (83.2, 94.6)
6 months	70.1 (51.1, 89.2)	82.1 (74.2, 89.9)
9 months	70.1 (51.1, 89.2)	72.8 (61.8, 83.9)
12 months	70.1 (51.1, 89.2)	72.8 (61.8, 83.9)
18 months	NE (NE, NE)	72.8 (61.8, 83.9)
Median Follow-up Time (months)	2.86	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
Deaths (Grade 5 TEAEs)
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	37 (23.9)	40 (11.9)
Number of Subjects Censored, n (%)	118 (76.1)	295 (88.1)
Time to first TEAE (months)		
25% percentile (95% CI)	3.19 (2.23, NE)	12.22 (8.21, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 6.8*	0.6, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.278 (0.248)
95% CI		(0.171, 0.452)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
Deaths (Grade 5 TEAEs)
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.3 (68.0, 82.5)	92.9 (90.1, 95.7)
6 months	68.4 (57.1, 79.8)	85.7 (80.7, 90.6)
9 months	NE (NE, NE)	79.2 (71.0, 87.3)
12 months	NE (NE, NE)	75.7 (65.5, 85.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3O
Summary of Time to Onset of Overall TEAE by Liver Metastases
Safety Population
Deaths (Grade 5 TEAEs)
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	8 (10.7)	8 (6.6)
Number of Subjects Censored, n (%)	67 (89.3)	113 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.98, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.8, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.409 (0.512)
95% CI		(0.150, 1.116)
Log-rank p-value		0.065

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.2 (83.3, 97.1)	96.5 (93.2, 99.9)
6 months	85.9 (75.4, 96.4)	91.5 (85.8, 97.3)
9 months	85.9 (75.4, 96.4)	91.5 (85.8, 97.3)
12 months	85.9 (75.4, 96.4)	91.5 (85.8, 97.3)
18 months	NE (NE, NE)	91.5 (85.8, 97.3)
Median Follow-up Time (months)	2.86	4.67

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	11 (100.0)	20 (95.2)
Number of Subjects Censored, n (%)	0	1 (4.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.30)	0.07 (0.03, 0.20)
Median (95% CI)	0.30 (0.03, 0.69)	0.36 (0.07, 0.69)
75% percentile (95% CI)	0.69 (0.20, NE)	0.69 (0.46, 1.35)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Min, Max	0.0, 1.6	0.0, 3.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.750 (0.473)
95% CI		(0.297, 1.893)
Log-rank p-value		0.476

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	0.0 (NE, NE)	4.8 (0.0, 13.9)
6 months	0.0 (NE, NE)	NE (NE, NE)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.30	0.36

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	202 (92.2)	431 (99.1)
Number of Subjects Censored, n (%)	17 (7.8)	4 (0.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.10 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.39, 0.59)	0.26 (0.23, 0.30)
75% percentile (95% CI)	0.72 (0.69, 0.92)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.438 (0.087)
95% CI		(1.213, 1.705)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	8.1 (4.5, 11.8)	1.6 (0.4, 2.8)
6 months	NE (NE, NE)	0.6 (0.0, 1.5)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Serious TEAE
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	4 (36.4)	9 (42.9)
Number of Subjects Censored, n (%)	7 (63.6)	12 (57.1)
Time to first TEAE (months)		
25% percentile (95% CI)	1.28 (0.69, NE)	3.25 (0.23, 4.07)
Median (95% CI)	NE (0.69, NE)	4.21 (3.25, NE)
75% percentile (95% CI)	NE (2.40, NE)	NE (4.21, NE)
Min, Max	0.7, 6.5*	0.2, 7.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.395 (0.776)
95% CI		(0.086, 1.807)
Log-rank p-value		0.210

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Serious TEAE
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	58.2 (25.1, 91.2)	76.2 (58.0, 94.4)
6 months	58.2 (25.1, 91.2)	46.6 (21.1, 72.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Serious TEAE
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	84 (38.4)	162 (37.2)
Number of Subjects Censored, n (%)	135 (61.6)	273 (62.8)
Time to first TEAE (months)		
25% percentile (95% CI)	1.31 (0.99, 1.94)	2.73 (1.97, 3.25)
Median (95% CI)	NE (3.65, NE)	9.23 (7.79, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.680 (0.139)
95% CI		(0.518, 0.893)
Log-rank p-value		0.008

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Serious TEAE
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	63.5 (57.0, 70.0)	72.0 (67.7, 76.3)
6 months	51.8 (40.8, 62.9)	59.6 (54.2, 65.1)
9 months	51.8 (40.8, 62.9)	51.2 (44.1, 58.2)
12 months	51.8 (40.8, 62.9)	42.8 (31.8, 53.8)
18 months	NE (NE, NE)	42.8 (31.8, 53.8)
Median Follow-up Time (months)	2.79	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE ≤ CTCAE Grade 2
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	10 (90.9)	20 (95.2)
Number of Subjects Censored, n (%)	1 (9.1)	1 (4.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.30)	0.07 (0.03, 0.30)
Median (95% CI)	0.30 (0.03, 0.72)	0.46 (0.07, 0.69)
75% percentile (95% CI)	0.72 (0.20, NE)	0.69 (0.46, 1.35)
Min, Max	0.0, 1.6	0.0, 3.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.899 (0.494)
95% CI		(0.341, 2.368)
Log-rank p-value		0.503

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE ≤ CTCAE Grade 2
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	0.0 (NE, NE)	4.8 (0.0, 13.9)
6 months	0.0 (NE, NE)	NE (NE, NE)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.30	0.46

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE ≤ CTCAE Grade 2
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	190 (86.8)	424 (97.5)
Number of Subjects Censored, n (%)	29 (13.2)	11 (2.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.10 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.56 (0.46, 0.69)	0.30 (0.23, 0.39)
75% percentile (95% CI)	0.76 (0.69, 1.25)	0.69 (NE, NE)
Min, Max	0.0, 4.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.464 (0.089)
95% CI		(1.230, 1.742)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE ≤ CTCAE Grade 2
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	11.7 (7.2, 16.1)	2.3 (0.8, 3.8)
6 months	NE (NE, NE)	0.9 (0.0, 2.1)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.56	0.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE ≥ CTCAE Grade 3
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	5 (45.5)	12 (57.1)
Number of Subjects Censored, n (%)	6 (54.5)	9 (42.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.72 (0.69, NE)	1.28 (0.20, 1.61)
Median (95% CI)	NE (0.69, NE)	3.25 (1.28, NE)
75% percentile (95% CI)	NE (2.00, NE)	NE (3.25, NE)
Min, Max	0.7, 6.5*	0.2, 7.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.483 (0.680)
95% CI		(0.127, 1.834)
Log-rank p-value		0.225

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE ≥ CTCAE Grade 3
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	50.9 (19.1, 82.8)	52.4 (31.0, 73.7)
6 months	50.9 (19.1, 82.8)	38.8 (15.9, 61.7)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE ≥ CTCAE Grade 3
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	111 (50.7)	274 (63.0)
Number of Subjects Censored, n (%)	108 (49.3)	161 (37.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.72, 1.25)	0.95 (0.69, 1.18)
Median (95% CI)	3.61 (2.27, 4.83)	2.79 (2.53, 3.61)
75% percentile (95% CI)	9.26 (5.36, NE)	8.90 (7.33, NE)
Min, Max	0.1, 9.3	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.087 (0.115)
95% CI		(0.868, 1.360)
Log-rank p-value		0.358

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE ≥ CTCAE Grade 3
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	54.3 (47.6, 60.9)	48.2 (43.4, 52.9)
6 months	31.0 (18.2, 43.8)	34.1 (28.9, 39.3)
9 months	31.0 (18.2, 43.8)	24.5 (18.2, 30.8)
12 months	0.0 (NE, NE)	18.0 (9.8, 26.1)
18 months	0.0 (NE, NE)	12.0 (1.0, 23.0)
Median Follow-up Time (months)	2.37	2.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Discontinuation due to TEAE
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	4 (36.4)	4 (19.0)
Number of Subjects Censored, n (%)	7 (63.6)	17 (81.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.66, NE)	8.21 (0.59, NE)
Median (95% CI)	NE (0.69, NE)	8.21 (8.21, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (8.21, NE)
Min, Max	0.7, 6.5*	0.6, 8.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.055 (1.075)
95% CI		(0.007, 0.455)
Log-rank p-value		0.004

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Discontinuation due to TEAE
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	63.6 (35.2, 92.1)	90.2 (77.3, 100.0)
6 months	63.6 (35.2, 92.1)	82.0 (62.7, 100.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.37

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Discontinuation due to TEAE
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	45 (20.5)	89 (20.5)
Number of Subjects Censored, n (%)	174 (79.5)	346 (79.5)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (3.15, NE)	7.03 (5.32, 8.90)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.658 (0.191)
95% CI		(0.453, 0.957)
Log-rank p-value		0.036

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Discontinuation due to TEAE
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.2 (77.0, 87.3)	86.4 (83.1, 89.6)
6 months	65.2 (52.3, 78.0)	78.5 (73.8, 83.1)
9 months	65.2 (52.3, 78.0)	68.2 (61.0, 75.3)
12 months	65.2 (52.3, 78.0)	63.4 (54.1, 72.7)
18 months	NE (NE, NE)	63.4 (54.1, 72.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Deaths (Grade 5 TEAEs)
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	2 (18.2)	1 (4.8)
Number of Subjects Censored, n (%)	9 (81.8)	20 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.02, NE)	NE (0.99, NE)
Median (95% CI)	NE (1.28, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 6.5*	1.0, 9.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.000 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.016

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Deaths (Grade 5 TEAEs)
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.8 (59.0, 100.0)	95.2 (86.1, 100.0)
6 months	81.8 (59.0, 100.0)	95.2 (86.1, 100.0)
9 months	NE (NE, NE)	95.2 (86.1, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	4.57

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3P
Summary of Time to Onset of Overall TEAE by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Deaths (Grade 5 TEAEs)
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	43 (19.6)	47 (10.8)
Number of Subjects Censored, n (%)	176 (80.4)	388 (89.2)
Time to first TEAE (months)		
25% percentile (95% CI)	3.98 (2.60, NE)	NE (9.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.350 (0.221)
95% CI		(0.227, 0.541)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE
Single

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.3 (74.8, 85.9)	93.8 (91.4, 96.1)
6 months	74.7 (66.5, 82.8)	87.0 (83.0, 91.0)
9 months	74.7 (66.5, 82.8)	82.8 (77.0, 88.6)
12 months	74.7 (66.5, 82.8)	80.6 (73.6, 87.6)
18 months	NE (NE, NE)	75.2 (63.1, 87.3)
Median Follow-up Time (months)	2.83	3.94

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	40 (88.9)	58 (96.7)
Number of Subjects Censored, n (%)	5 (11.1)	2 (3.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.23)	0.13 (0.07, 0.26)
Median (95% CI)	0.53 (0.23, 0.69)	0.38 (0.26, 0.56)
75% percentile (95% CI)	0.69 (0.69, 1.94)	0.69 (0.56, 0.69)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Min, Max	0.0, 3.6	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.372 (0.228)
95% CI		(0.877, 2.146)
Log-rank p-value		0.140

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	13.3 (3.4, 23.3)	5.0 (0.0, 10.5)
6 months	0.0 (NE, NE)	2.5 (0.0, 6.9)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.53	0.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	172 (93.5)	393 (99.2)
Number of Subjects Censored, n (%)	12 (6.5)	3 (0.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.11 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.39, 0.59)	0.23 (0.20, 0.30)
75% percentile (95% CI)	0.71 (0.69, 0.82)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.412 (0.093)
95% CI		(1.176, 1.694)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	6.4 (2.8, 9.9)	1.3 (0.2, 2.4)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Serious TEAE
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	13 (28.9)	13 (21.7)
Number of Subjects Censored, n (%)	32 (71.1)	47 (78.3)
Time to first TEAE (months)		
25% percentile (95% CI)	2.30 (1.15, NE)	NE (2.66, NE)
Median (95% CI)	NE (3.65, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.586 (0.439)
95% CI		(0.248, 1.384)
Log-rank p-value		0.268

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Serious TEAE
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.9 (59.8, 86.0)	83.1 (73.5, 92.7)
6 months	65.6 (47.6, 83.6)	76.3 (64.8, 87.8)
9 months	65.6 (47.6, 83.6)	76.3 (64.8, 87.8)
12 months	65.6 (47.6, 83.6)	76.3 (64.8, 87.8)
18 months	NE (NE, NE)	76.3 (64.8, 87.8)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Serious TEAE
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	74 (40.2)	158 (39.9)
Number of Subjects Censored, n (%)	110 (59.8)	238 (60.1)
Time to first TEAE (months)		
25% percentile (95% CI)	1.23 (0.92, 1.81)	2.53 (1.84, 2.96)
Median (95% CI)	NE (3.19, NE)	7.82 (6.01, 11.96)
75% percentile (95% CI)	NE (NE, NE)	18.04 (11.96, NE)
Min, Max	0.1, 8.4*	0.1, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.684 (0.146)
95% CI		(0.515, 0.910)
Log-rank p-value		0.010

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Serious TEAE
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	60.8 (53.5, 68.0)	70.6 (66.0, 75.2)
6 months	50.0 (37.8, 62.3)	56.3 (50.5, 62.2)
9 months	NE (NE, NE)	46.7 (39.0, 54.4)
12 months	NE (NE, NE)	36.8 (24.6, 49.1)
18 months	NE (NE, NE)	36.8 (24.6, 49.1)
Median Follow-up Time (months)	2.46	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE ≤ CTCAE Grade 2
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	39 (86.7)	58 (96.7)
Number of Subjects Censored, n (%)	6 (13.3)	2 (3.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.23)	0.15 (0.07, 0.26)
Median (95% CI)	0.53 (0.23, 0.69)	0.39 (0.26, 0.62)
75% percentile (95% CI)	0.76 (0.69, 1.94)	0.69 (0.62, 0.72)
Min, Max	0.0, 4.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.372 (0.230)
95% CI		(0.874, 2.154)
Log-rank p-value		0.249

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE ≤ CTCAE Grade 2
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	13.3 (3.4, 23.3)	5.0 (0.0, 10.5)
6 months	NE (NE, NE)	2.5 (0.0, 6.9)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.53	0.39

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE ≤ CTCAE Grade 2
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	160 (87.0)	386 (97.5)
Number of Subjects Censored, n (%)	24 (13.0)	10 (2.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.11 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.54 (0.46, 0.69)	0.26 (0.23, 0.39)
75% percentile (95% CI)	0.76 (0.69, 1.25)	0.69 (NE, NE)
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.454 (0.096)
95% CI		(1.205, 1.753)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE ≤ CTCAE Grade 2
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	10.8 (6.0, 15.7)	1.9 (0.4, 3.4)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.54	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE ≥ CTCAE Grade 3
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	17 (37.8)	29 (48.3)
Number of Subjects Censored, n (%)	28 (62.2)	31 (51.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.81 (0.69, 4.83)	1.20 (0.69, 2.63)
Median (95% CI)	4.83 (3.65, NE)	5.19 (2.63, NE)
75% percentile (95% CI)	9.26 (4.83, NE)	NE (NE, NE)
Min, Max	0.2, 9.3	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.222 (0.341)
95% CI		(0.626, 2.383)
Log-rank p-value		0.458

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE ≥ CTCAE Grade 3
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	68.7 (55.0, 82.3)	59.4 (46.8, 72.0)
6 months	40.1 (5.4, 74.7)	45.8 (31.3, 60.4)
9 months	40.1 (5.4, 74.7)	45.8 (31.3, 60.4)
12 months	0.0 (NE, NE)	45.8 (31.3, 60.4)
18 months	0.0 (NE, NE)	45.8 (31.3, 60.4)
Median Follow-up Time (months)	2.83	2.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE ≥ CTCAE Grade 3
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	98 (53.3)	257 (64.9)
Number of Subjects Censored, n (%)	86 (46.7)	139 (35.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.92 (0.72, 1.02)	0.92 (0.69, 1.18)
Median (95% CI)	3.15 (1.94, 4.34)	2.69 (2.00, 3.25)
75% percentile (95% CI)	NE (5.36, NE)	7.62 (6.90, 11.96)
Min, Max	0.1, 6.8*	0.0, 16.1
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.049 (0.121)
95% CI		(0.827, 1.329)
Log-rank p-value		0.583

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE ≥ CTCAE Grade 3
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	50.4 (43.0, 57.7)	46.7 (41.8, 51.7)
6 months	30.1 (16.9, 43.3)	32.4 (27.0, 37.8)
9 months	NE (NE, NE)	21.0 (14.3, 27.8)
12 months	NE (NE, NE)	13.6 (5.1, 22.0)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.00	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Discontinuation due to TEAE
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	5 (11.1)	10 (16.7)
Number of Subjects Censored, n (%)	40 (88.9)	50 (83.3)
Time to first TEAE (months)		
25% percentile (95% CI)	4.83 (3.65, NE)	NE (2.76, NE)
Median (95% CI)	NE (4.83, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (4.83, NE)	NE (NE, NE)
Min, Max	0.7, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.858 (0.697)
95% CI		(0.474, 7.288)
Log-rank p-value		0.435

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Discontinuation due to TEAE
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.3 (86.0, 100.0)	86.4 (77.6, 95.2)
6 months	56.0 (9.5, 100.0)	81.8 (71.5, 92.2)
9 months	56.0 (9.5, 100.0)	81.8 (71.5, 92.2)
12 months	56.0 (9.5, 100.0)	81.8 (71.5, 92.2)
18 months	NE (NE, NE)	81.8 (71.5, 92.2)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Discontinuation due to TEAE
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	44 (23.9)	83 (21.0)
Number of Subjects Censored, n (%)	140 (76.1)	313 (79.0)
Time to first TEAE (months)		
25% percentile (95% CI)	3.19 (1.68, NE)	6.90 (5.26, 8.28)
Median (95% CI)	NE (NE, NE)	NE (11.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.552 (0.196)
95% CI		(0.376, 0.812)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Discontinuation due to TEAE
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.2 (72.2, 84.3)	86.6 (83.2, 90.0)
6 months	64.4 (51.7, 77.0)	78.1 (73.1, 83.1)
9 months	NE (NE, NE)	65.1 (57.0, 73.3)
12 months	NE (NE, NE)	59.7 (49.1, 70.2)
18 months	NE (NE, NE)	59.7 (49.1, 70.2)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Deaths (Grade 5 TEAEs)
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	5 (11.1)	2 (3.3)
Number of Subjects Censored, n (%)	40 (88.9)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.76, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.256 (0.951)
95% CI		(0.040, 1.648)
Log-rank p-value		0.154

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Deaths (Grade 5 TEAEs)
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.6 (77.4, 97.9)	98.1 (94.6, 100.0)
6 months	87.6 (77.4, 97.9)	95.8 (89.9, 100.0)
9 months	87.6 (77.4, 97.9)	95.8 (89.9, 100.0)
12 months	87.6 (77.4, 97.9)	95.8 (89.9, 100.0)
18 months	NE (NE, NE)	95.8 (89.9, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3Q
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Deaths (Grade 5 TEAEs)
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	40 (21.7)	46 (11.6)
Number of Subjects Censored, n (%)	144 (78.3)	350 (88.4)
Time to first TEAE (months)		
25% percentile (95% CI)	3.75 (2.33, NE)	12.22 (8.87, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.6, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.339 (0.228)
95% CI		(0.217, 0.531)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
TEAE
Single

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.5 (72.2, 84.7)	93.2 (90.7, 95.7)
6 months	71.3 (61.6, 81.0)	86.0 (81.7, 90.4)
9 months	NE (NE, NE)	81.3 (74.8, 87.7)
12 months	NE (NE, NE)	78.7 (70.8, 86.7)
18 months	NE (NE, NE)	72.2 (57.9, 86.5)
Median Follow-up Time (months)	2.83	3.75

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	37 (88.1)	58 (96.7)
Number of Subjects Censored, n (%)	5 (11.9)	2 (3.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.23)	0.13 (0.07, 0.26)
Median (95% CI)	0.59 (0.23, 0.69)	0.38 (0.26, 0.56)
75% percentile (95% CI)	0.92 (0.69, NE)	0.69 (0.56, 0.69)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
TEAE
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Min, Max	0.0, 3.6	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.498 (0.238)
95% CI		(0.940, 2.387)
Log-rank p-value		0.078

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
TEAE
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	14.3 (3.7, 24.9)	5.0 (0.0, 10.5)
6 months	0.0 (NE, NE)	2.5 (0.0, 6.9)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.59	0.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
TEAE
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	176 (93.6)	393 (99.2)
Number of Subjects Censored, n (%)	12 (6.4)	3 (0.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.11 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.39, 0.59)	0.23 (0.20, 0.30)
75% percentile (95% CI)	0.69 (0.69, 0.82)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.395 (0.092)
95% CI		(1.164, 1.671)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
TEAE
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	6.2 (2.8, 9.7)	1.3 (0.2, 2.4)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
Serious TEAE
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	13 (31.0)	13 (21.7)
Number of Subjects Censored, n (%)	29 (69.0)	47 (78.3)
Time to first TEAE (months)		
25% percentile (95% CI)	2.30 (1.15, NE)	NE (2.66, NE)
Median (95% CI)	NE (3.35, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.518 (0.441)
95% CI		(0.218, 1.228)
Log-rank p-value		0.165

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
Serious TEAE
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.3 (59.8, 86.9)	83.1 (73.5, 92.7)
6 months	58.7 (37.5, 79.8)	76.3 (64.8, 87.8)
9 months	58.7 (37.5, 79.8)	76.3 (64.8, 87.8)
12 months	58.7 (37.5, 79.8)	76.3 (64.8, 87.8)
18 months	NE (NE, NE)	76.3 (64.8, 87.8)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
Serious TEAE
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	75 (39.9)	158 (39.9)
Number of Subjects Censored, n (%)	113 (60.1)	238 (60.1)
Time to first TEAE (months)		
25% percentile (95% CI)	1.23 (0.92, 1.81)	2.53 (1.84, 2.96)
Median (95% CI)	NE (3.19, NE)	7.82 (6.01, 11.96)
75% percentile (95% CI)	NE (NE, NE)	18.04 (11.96, NE)
Min, Max	0.1, 8.4*	0.1, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.693 (0.145)
95% CI		(0.522, 0.920)
Log-rank p-value		0.013

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
Serious TEAE
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	61.1 (54.0, 68.2)	70.6 (66.0, 75.2)
6 months	50.6 (38.4, 62.7)	56.3 (50.5, 62.2)
9 months	NE (NE, NE)	46.7 (39.0, 54.4)
12 months	NE (NE, NE)	36.8 (24.6, 49.1)
18 months	NE (NE, NE)	36.8 (24.6, 49.1)
Median Follow-up Time (months)	2.51	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
TEAE ≤ CTCAE Grade 2
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	36 (85.7)	58 (96.7)
Number of Subjects Censored, n (%)	6 (14.3)	2 (3.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.23)	0.15 (0.07, 0.26)
Median (95% CI)	0.59 (0.23, 0.69)	0.39 (0.26, 0.62)
75% percentile (95% CI)	0.92 (0.69, NE)	0.69 (0.62, 0.72)
Min, Max	0.0, 4.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.458 (0.238)
95% CI		(0.915, 2.323)
Log-rank p-value		0.171

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
TEAE ≤ CTCAE Grade 2
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	14.3 (3.7, 24.9)	5.0 (0.0, 10.5)
6 months	NE (NE, NE)	2.5 (0.0, 6.9)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.59	0.39

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
TEAE ≤ CTCAE Grade 2
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	164 (87.2)	386 (97.5)
Number of Subjects Censored, n (%)	24 (12.8)	10 (2.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.11 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.54 (0.46, 0.66)	0.26 (0.23, 0.39)
75% percentile (95% CI)	0.76 (0.69, 1.15)	0.69 (NE, NE)
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.441 (0.095)
95% CI		(1.197, 1.734)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
TEAE ≤ CTCAE Grade 2
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	10.6 (5.9, 15.4)	1.9 (0.4, 3.4)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.54	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
TEAE ≥ CTCAE Grade 3
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	17 (40.5)	29 (48.3)
Number of Subjects Censored, n (%)	25 (59.5)	31 (51.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.81 (0.69, 3.65)	1.20 (0.69, 2.63)
Median (95% CI)	4.83 (3.35, NE)	5.19 (2.63, NE)
75% percentile (95% CI)	9.26 (4.83, NE)	NE (NE, NE)
Min, Max	0.2, 9.3	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.104 (0.342)
95% CI		(0.565, 2.157)
Log-rank p-value		0.700

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
TEAE ≥ CTCAE Grade 3
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	68.8 (54.7, 82.9)	59.4 (46.8, 72.0)
6 months	34.4 (2.8, 66.0)	45.8 (31.3, 60.4)
9 months	34.4 (2.8, 66.0)	45.8 (31.3, 60.4)
12 months	0.0 (NE, NE)	45.8 (31.3, 60.4)
18 months	0.0 (NE, NE)	45.8 (31.3, 60.4)
Median Follow-up Time (months)	2.83	2.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
TEAE ≥ CTCAE Grade 3
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	99 (52.7)	257 (64.9)
Number of Subjects Censored, n (%)	89 (47.3)	139 (35.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.92 (0.72, 1.02)	0.92 (0.69, 1.18)
Median (95% CI)	3.15 (1.94, 4.34)	2.69 (2.00, 3.25)
75% percentile (95% CI)	NE (5.36, NE)	7.62 (6.90, 11.96)
Min, Max	0.1, 6.8*	0.0, 16.1
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.065 (0.120)
95% CI		(0.841, 1.348)
Log-rank p-value		0.498

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
TEAE ≥ CTCAE Grade 3
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	50.9 (43.7, 58.1)	46.7 (41.8, 51.7)
6 months	30.7 (17.4, 44.0)	32.4 (27.0, 37.8)
9 months	NE (NE, NE)	21.0 (14.3, 27.8)
12 months	NE (NE, NE)	13.6 (5.1, 22.0)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.02	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
Discontinuation due to TEAE
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	5 (11.9)	10 (16.7)
Number of Subjects Censored, n (%)	37 (88.1)	50 (83.3)
Time to first TEAE (months)		
25% percentile (95% CI)	4.83 (3.65, NE)	NE (2.76, NE)
Median (95% CI)	NE (4.83, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (4.83, NE)	NE (NE, NE)
Min, Max	0.7, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.742 (0.698)
95% CI		(0.444, 6.839)
Log-rank p-value		0.444

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
Discontinuation due to TEAE
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (85.1, 100.0)	86.4 (77.6, 95.2)
6 months	62.7 (24.6, 100.0)	81.8 (71.5, 92.2)
9 months	62.7 (24.6, 100.0)	81.8 (71.5, 92.2)
12 months	62.7 (24.6, 100.0)	81.8 (71.5, 92.2)
18 months	NE (NE, NE)	81.8 (71.5, 92.2)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
Discontinuation due to TEAE
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	44 (23.4)	83 (21.0)
Number of Subjects Censored, n (%)	144 (76.6)	313 (79.0)
Time to first TEAE (months)		
25% percentile (95% CI)	3.98 (1.71, NE)	6.90 (5.26, 8.28)
Median (95% CI)	NE (NE, NE)	NE (11.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.568 (0.196)
95% CI		(0.387, 0.835)
Log-rank p-value		0.004

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
Discontinuation due to TEAE
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.7 (72.7, 84.7)	86.6 (83.2, 90.0)
6 months	65.0 (52.4, 77.6)	78.1 (73.1, 83.1)
9 months	NE (NE, NE)	65.1 (57.0, 73.3)
12 months	NE (NE, NE)	59.7 (49.1, 70.2)
18 months	NE (NE, NE)	59.7 (49.1, 70.2)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
Deaths (Grade 5 TEAEs)
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	4 (9.5)	2 (3.3)
Number of Subjects Censored, n (%)	38 (90.5)	58 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.30, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.274 (1.001)
95% CI		(0.039, 1.952)
Log-rank p-value		0.201

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
Deaths (Grade 5 TEAEs)
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.7 (80.1, 99.3)	98.1 (94.6, 100.0)
6 months	89.7 (80.1, 99.3)	95.8 (89.9, 100.0)
9 months	89.7 (80.1, 99.3)	95.8 (89.9, 100.0)
12 months	89.7 (80.1, 99.3)	95.8 (89.9, 100.0)
18 months	NE (NE, NE)	95.8 (89.9, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3R
Summary of Time to Onset of Overall TEAE by Number of Metastatic Tumor Sites
Safety Population
Deaths (Grade 5 TEAEs)
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	41 (21.8)	46 (11.6)
Number of Subjects Censored, n (%)	147 (78.2)	350 (88.4)
Time to first TEAE (months)		
25% percentile (95% CI)	3.75 (2.37, NE)	12.22 (8.87, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.6, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.339 (0.227)
95% CI		(0.217, 0.528)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
TEAE
< 18.5

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.2 (72.0, 84.4)	93.2 (90.7, 95.7)
6 months	71.3 (61.8, 80.8)	86.0 (81.7, 90.4)
9 months	NE (NE, NE)	81.3 (74.8, 87.7)
12 months	NE (NE, NE)	78.7 (70.8, 86.7)
18 months	NE (NE, NE)	72.2 (57.9, 86.5)
Median Follow-up Time (months)	2.83	3.75

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	14 (100.0)	20 (100.0)
Number of Subjects Censored, n (%)	0	0
Time to first TEAE (months)		
25% percentile (95% CI)	0.16 (0.03, 0.33)	0.11 (0.03, 0.26)
Median (95% CI)	0.36 (0.03, 0.69)	0.33 (0.10, 0.69)
75% percentile (95% CI)	0.69 (0.33, NE)	0.69 (0.36, 0.82)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
TEAE
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Min, Max	0.0, 1.6	0.0, 1.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.249 (0.401)
95% CI		(0.568, 2.742)
Log-rank p-value		0.678

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
TEAE
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	0.0 (NE, NE)	0.0 (NE, NE)
6 months	0.0 (NE, NE)	0.0 (NE, NE)
9 months	0.0 (NE, NE)	0.0 (NE, NE)
12 months	0.0 (NE, NE)	0.0 (NE, NE)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.36	0.33

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
TEAE
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	70 (92.1)	138 (98.6)
Number of Subjects Censored, n (%)	6 (7.9)	2 (1.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.20 (0.07, 0.30)	0.10 (0.07, 0.10)
Median (95% CI)	0.53 (0.36, 0.69)	0.23 (0.16, 0.36)
75% percentile (95% CI)	0.72 (0.69, 1.35)	0.67 (0.46, 0.69)
Min, Max	0.0, 3.6	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.613 (0.154)
95% CI		(1.193, 2.180)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
TEAE
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	9.2 (2.7, 15.7)	1.4 (0.0, 3.4)
6 months	0.0 (NE, NE)	1.4 (0.0, 3.4)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.53	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
TEAE
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	124 (91.9)	282 (98.9)
Number of Subjects Censored, n (%)	11 (8.1)	3 (1.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.13)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.30, 0.62)	0.26 (0.23, 0.36)
75% percentile (95% CI)	0.69 (0.69, 0.95)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.314 (0.111)
95% CI		(1.058, 1.634)
Log-rank p-value		0.020

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
TEAE
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	8.0 (3.4, 12.6)	2.1 (0.4, 3.8)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
Serious TEAE
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	4 (28.6)	14 (70.0)
Number of Subjects Censored, n (%)	10 (71.4)	6 (30.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.94 (0.39, NE)	1.40 (0.16, 1.84)
Median (95% CI)	NE (1.68, NE)	2.68 (1.35, 8.28)
75% percentile (95% CI)	NE (NE, NE)	8.28 (2.69, NE)
Min, Max	0.4, 4.1*	0.2, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.431 (0.636)
95% CI		(0.699, 8.448)
Log-rank p-value		0.276

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
Serious TEAE
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	69.8 (44.8, 94.8)	39.4 (17.7, 61.1)
6 months	NE (NE, NE)	32.8 (11.3, 54.4)
9 months	NE (NE, NE)	21.9 (0.0, 44.5)
12 months	NE (NE, NE)	21.9 (0.0, 44.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
Serious TEAE
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	30 (39.5)	63 (45.0)
Number of Subjects Censored, n (%)	46 (60.5)	77 (55.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.30 (0.72, 2.27)	1.71 (1.41, 2.69)
Median (95% CI)	NE (2.37, NE)	7.75 (4.04, 9.23)
75% percentile (95% CI)	NE (NE, NE)	11.96 (8.90, NE)
Min, Max	0.2, 8.4*	0.1, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.949 (0.232)
95% CI		(0.602, 1.495)
Log-rank p-value		0.854

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
Serious TEAE
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	60.3 (49.0, 71.7)	63.9 (55.7, 72.1)
6 months	56.5 (43.7, 69.4)	52.4 (42.7, 62.2)
9 months	NE (NE, NE)	39.4 (24.6, 54.3)
12 months	NE (NE, NE)	22.5 (1.5, 43.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.43	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
Serious TEAE
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	52 (38.5)	92 (32.3)
Number of Subjects Censored, n (%)	83 (61.5)	193 (67.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.22 (0.92, 2.00)	3.29 (2.76, 4.47)
Median (95% CI)	5.36 (3.35, NE)	18.04 (7.82, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.525 (0.182)
95% CI		(0.367, 0.749)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
Serious TEAE
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	64.6 (56.5, 72.8)	78.4 (73.5, 83.2)
6 months	45.0 (25.9, 64.1)	63.3 (56.5, 70.0)
9 months	45.0 (25.9, 64.1)	57.1 (49.1, 65.1)
12 months	45.0 (25.9, 64.1)	51.4 (38.5, 64.2)
18 months	NE (NE, NE)	51.4 (38.5, 64.2)
Median Follow-up Time (months)	2.79	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
TEAE ≤ CTCAE Grade 2
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	14 (100.0)	20 (100.0)
Number of Subjects Censored, n (%)	0	0
Time to first TEAE (months)		
25% percentile (95% CI)	0.16 (0.03, 0.33)	0.18 (0.03, 0.30)
Median (95% CI)	0.36 (0.03, 0.69)	0.41 (0.13, 0.69)
75% percentile (95% CI)	0.69 (0.33, NE)	0.69 (0.46, 0.82)
Min, Max	0.0, 1.6	0.0, 1.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.171 (0.406)
95% CI		(0.528, 2.595)
Log-rank p-value		0.549

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
TEAE ≤ CTCAE Grade 2
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	0.0 (NE, NE)	0.0 (NE, NE)
6 months	0.0 (NE, NE)	0.0 (NE, NE)
9 months	0.0 (NE, NE)	0.0 (NE, NE)
12 months	0.0 (NE, NE)	0.0 (NE, NE)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.36	0.41

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
TEAE ≤ CTCAE Grade 2
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	63 (82.9)	137 (97.9)
Number of Subjects Censored, n (%)	13 (17.1)	3 (2.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.20 (0.07, 0.30)	0.10 (0.07, 0.13)
Median (95% CI)	0.62 (0.39, 0.69)	0.26 (0.20, 0.43)
75% percentile (95% CI)	0.92 (0.69, 2.76)	0.69 (0.59, 0.69)
Min, Max	0.0, 4.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.737 (0.158)
95% CI		(1.274, 2.369)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
TEAE ≤ CTCAE Grade 2
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	14.3 (5.8, 22.8)	1.5 (0.0, 3.6)
6 months	NE (NE, NE)	1.5 (0.0, 3.6)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.61	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
TEAE ≤ CTCAE Grade 2
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	118 (87.4)	276 (96.8)
Number of Subjects Censored, n (%)	17 (12.6)	9 (3.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.13)	0.07 (0.07, 0.10)
Median (95% CI)	0.49 (0.33, 0.69)	0.30 (0.23, 0.39)
75% percentile (95% CI)	0.72 (0.69, 1.15)	0.69 (NE, NE)
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.304 (0.113)
95% CI		(1.046, 1.626)
Log-rank p-value		0.028

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
TEAE ≤ CTCAE Grade 2
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	11.6 (6.0, 17.2)	3.2 (1.0, 5.4)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.49	0.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
TEAE ≥ CTCAE Grade 3
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	7 (50.0)	17 (85.0)
Number of Subjects Censored, n (%)	7 (50.0)	3 (15.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.39, 1.94)	0.66 (0.03, 1.35)
Median (95% CI)	1.94 (0.69, NE)	1.49 (0.62, 2.69)
75% percentile (95% CI)	NE (1.94, NE)	2.69 (1.61, NE)
Min, Max	0.4, 2.9*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.430 (0.473)
95% CI		(0.566, 3.614)
Log-rank p-value		0.643

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
TEAE ≥ CTCAE Grade 3
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	NE (NE, NE)	20.0 (2.5, 37.5)
6 months	NE (NE, NE)	10.0 (0.0, 26.4)
9 months	NE (NE, NE)	10.0 (0.0, 26.4)
12 months	NE (NE, NE)	10.0 (0.0, 26.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.87	1.49

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
TEAE ≥ CTCAE Grade 3
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	39 (51.3)	93 (66.4)
Number of Subjects Censored, n (%)	37 (48.7)	47 (33.6)
Time to first TEAE (months)		
25% percentile (95% CI)	1.13 (0.66, 1.54)	0.87 (0.53, 1.25)
Median (95% CI)	3.65 (1.87, NE)	2.53 (1.68, 3.61)
75% percentile (95% CI)	NE (5.55, NE)	7.33 (5.59, NE)
Min, Max	0.2, 6.8*	0.1, 12.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.237 (0.198)
95% CI		(0.839, 1.822)
Log-rank p-value		0.257

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
TEAE ≥ CTCAE Grade 3
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	51.8 (40.4, 63.2)	45.7 (37.3, 54.1)
6 months	37.7 (21.1, 54.3)	31.2 (22.0, 40.3)
9 months	NE (NE, NE)	18.7 (7.0, 30.5)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.25	2.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
TEAE ≥ CTCAE Grade 3
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	65 (48.1)	171 (60.0)
Number of Subjects Censored, n (%)	70 (51.9)	114 (40.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.72, 1.35)	0.95 (0.69, 1.31)
Median (95% CI)	3.61 (2.33, 5.36)	3.25 (2.53, 4.27)
75% percentile (95% CI)	9.26 (4.83, NE)	11.04 (7.39, NE)
Min, Max	0.1, 9.3	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.049 (0.149)
95% CI		(0.783, 1.406)
Log-rank p-value		0.564

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
TEAE ≥ CTCAE Grade 3
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	58.1 (49.7, 66.5)	51.3 (45.4, 57.1)
6 months	27.9 (8.3, 47.5)	36.8 (30.3, 43.3)
9 months	27.9 (8.3, 47.5)	27.2 (19.3, 35.1)
12 months	0.0 (NE, NE)	23.4 (13.6, 33.1)
18 months	0.0 (NE, NE)	15.6 (1.5, 29.6)
Median Follow-up Time (months)	2.69	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
Discontinuation due to TEAE
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	3 (21.4)	6 (30.0)
Number of Subjects Censored, n (%)	11 (78.6)	14 (70.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.39, NE)	5.03 (0.30, NE)
Median (95% CI)	NE (0.95, NE)	9.69 (5.03, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (9.69, NE)
Min, Max	0.4, 4.1*	0.3, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.684 (0.827)
95% CI		(0.135, 3.457)
Log-rank p-value		0.621

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
Discontinuation due to TEAE
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.6 (57.1, 100.0)	79.7 (61.9, 97.5)
6 months	NE (NE, NE)	68.3 (42.6, 94.0)
9 months	NE (NE, NE)	68.3 (42.6, 94.0)
12 months	NE (NE, NE)	45.5 (5.3, 85.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
Discontinuation due to TEAE
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	15 (19.7)	26 (18.6)
Number of Subjects Censored, n (%)	61 (80.3)	114 (81.4)
Time to first TEAE (months)		
25% percentile (95% CI)	3.98 (1.54, NE)	8.28 (4.17, NE)
Median (95% CI)	NE (4.34, NE)	NE (8.90, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.1, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.685 (0.342)
95% CI		(0.351, 1.339)
Log-rank p-value		0.320

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
Discontinuation due to TEAE
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.0 (75.6, 92.3)	88.3 (82.9, 93.7)
6 months	67.5 (49.3, 85.7)	79.9 (71.8, 88.0)
9 months	NE (NE, NE)	64.6 (48.5, 80.8)
12 months	NE (NE, NE)	64.6 (48.5, 80.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
Discontinuation due to TEAE
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	29 (21.5)	58 (20.4)
Number of Subjects Censored, n (%)	106 (78.5)	227 (79.6)
Time to first TEAE (months)		
25% percentile (95% CI)	4.57 (1.81, NE)	7.46 (5.32, NE)
Median (95% CI)	NE (4.83, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.594 (0.240)
95% CI		(0.371, 0.952)
Log-rank p-value		0.045

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
Discontinuation due to TEAE
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.8 (74.0, 87.6)	86.4 (82.4, 90.4)
6 months	64.2 (46.7, 81.6)	78.8 (73.3, 84.4)
9 months	64.2 (46.7, 81.6)	69.4 (61.1, 77.7)
12 months	64.2 (46.7, 81.6)	64.4 (52.3, 76.6)
18 months	NE (NE, NE)	64.4 (52.3, 76.6)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
Deaths (Grade 5 TEAEs)
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	3 (21.4)	8 (40.0)
Number of Subjects Censored, n (%)	11 (78.6)	12 (60.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.89, NE)	2.66 (0.62, 9.69)
Median (95% CI)	NE (1.94, NE)	9.69 (2.66, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (9.69, NE)
Min, Max	0.9, 4.1*	0.6, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.938 (0.753)
95% CI		(0.215, 4.102)
Log-rank p-value		0.893

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
Deaths (Grade 5 TEAEs)
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.7 (51.3, 100.0)	73.1 (52.9, 93.4)
6 months	NE (NE, NE)	56.4 (30.5, 82.3)
9 months	NE (NE, NE)	56.4 (30.5, 82.3)
12 months	NE (NE, NE)	37.6 (2.9, 72.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
Deaths (Grade 5 TEAEs)
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	17 (22.4)	19 (13.6)
Number of Subjects Censored, n (%)	59 (77.6)	121 (86.4)
Time to first TEAE (months)		
25% percentile (95% CI)	3.98 (2.23, NE)	12.22 (5.95, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.8, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.440 (0.360)
95% CI		(0.217, 0.892)
Log-rank p-value		0.031

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
Deaths (Grade 5 TEAEs)
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.6 (66.4, 86.8)	92.0 (87.4, 96.5)
6 months	71.5 (57.9, 85.1)	84.4 (76.6, 92.3)
9 months	NE (NE, NE)	76.1 (62.2, 89.9)
12 months	NE (NE, NE)	76.1 (62.2, 89.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.1.3S
Summary of Time to Onset of Overall TEAE by Body Mass Index
Safety Population
Deaths (Grade 5 TEAEs)
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	24 (17.8)	21 (7.4)
Number of Subjects Censored, n (%)	111 (82.2)	264 (92.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.19, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.252 (0.321)
95% CI		(0.134, 0.472)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
TEAE
<65 years

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.9 (76.3, 89.4)	96.0 (93.7, 98.3)
6 months	77.1 (67.2, 87.1)	90.6 (86.3, 94.9)
9 months	77.1 (67.2, 87.1)	87.9 (82.2, 93.6)
12 months	77.1 (67.2, 87.1)	87.9 (82.2, 93.6)
18 months	NE (NE, NE)	87.9 (82.2, 93.6)
Median Follow-up Time (months)	2.83	4.24

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	108 (91.5)	240 (98.4)
Number of Subjects Censored, n (%)	10 (8.5)	4 (1.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.13 (0.07, 0.23)	0.10 (0.07, 0.13)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
TEAE
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Median (95% CI)	0.46 (0.36, 0.66)	0.30 (0.23, 0.46)
75% percentile (95% CI)	0.72 (0.69, 1.02)	0.69 (NE, NE)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.370 (0.120)
95% CI		(1.083, 1.733)
Log-rank p-value		0.009

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
TEAE
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	8.5 (3.4, 13.5)	2.0 (0.3, 3.8)
6 months	NE (NE, NE)	1.4 (0.0, 3.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
TEAE
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	103 (92.0)	210 (99.1)
Number of Subjects Censored, n (%)	9 (8.0)	2 (0.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.20)	0.07 (NE, NE)
Median (95% CI)	0.46 (0.30, 0.66)	0.23 (0.16, 0.30)
75% percentile (95% CI)	0.69 (0.69, 0.92)	0.69 (0.49, 0.69)
Min, Max	0.0, 3.6	0.0, 3.7
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.454 (0.123)
95% CI		(1.142, 1.852)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
TEAE
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	8.4 (3.1, 13.6)	1.9 (0.1, 3.7)
6 months	0.0 (NE, NE)	0.0 (NE, NE)
9 months	0.0 (NE, NE)	0.0 (NE, NE)
12 months	0.0 (NE, NE)	0.0 (NE, NE)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.46	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
Serious TEAE
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	34 (28.8)	87 (35.7)
Number of Subjects Censored, n (%)	84 (71.2)	157 (64.3)
Time to first TEAE (months)		
25% percentile (95% CI)	1.81 (1.02, NE)	2.96 (1.87, 4.04)
Median (95% CI)	NE (NE, NE)	11.04 (7.03, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (11.04, NE)
Min, Max	0.1, 6.8*	0.1, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.872 (0.209)
95% CI		(0.578, 1.314)
Log-rank p-value		0.652

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
Serious TEAE
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.1 (62.7, 79.4)	74.5 (68.9, 80.1)
6 months	67.1 (56.2, 78.0)	60.7 (53.4, 68.1)
9 months	NE (NE, NE)	50.1 (40.2, 60.0)
12 months	NE (NE, NE)	41.7 (24.7, 58.8)
18 months	NE (NE, NE)	41.7 (24.7, 58.8)
Median Follow-up Time (months)	2.83	3.19

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
Serious TEAE
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	38 (33.9)	67 (31.6)
Number of Subjects Censored, n (%)	74 (66.1)	145 (68.4)
Time to first TEAE (months)		
25% percentile (95% CI)	1.54 (0.92, 3.15)	2.83 (1.87, 4.50)
Median (95% CI)	5.36 (3.35, NE)	11.96 (8.90, NE)
75% percentile (95% CI)	NE (5.36, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.681 (0.210)
95% CI		(0.451, 1.029)
Log-rank p-value		0.083

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
Serious TEAE
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	68.4 (59.5, 77.3)	73.7 (67.6, 79.8)
6 months	45.5 (22.6, 68.5)	66.2 (58.8, 73.5)
9 months	45.5 (22.6, 68.5)	59.4 (49.3, 69.5)
12 months	45.5 (22.6, 68.5)	49.1 (32.8, 65.4)
18 months	NE (NE, NE)	49.1 (32.8, 65.4)
Median Follow-up Time (months)	2.58	3.48

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
TEAE ≤ CTCAE Grade 2
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	104 (88.1)	238 (97.5)
Number of Subjects Censored, n (%)	14 (11.9)	6 (2.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.13 (0.07, 0.26)	0.10 (0.07, 0.13)
Median (95% CI)	0.53 (0.39, 0.69)	0.36 (0.26, 0.49)
75% percentile (95% CI)	0.82 (0.69, 1.38)	0.69 (NE, NE)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.388 (0.121)
95% CI		(1.094, 1.760)
Log-rank p-value		0.007

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
TEAE ≤ CTCAE Grade 2
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	10.8 (5.0, 16.6)	2.3 (0.4, 4.3)
6 months	NE (NE, NE)	1.6 (0.0, 3.4)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.53	0.36

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
TEAE ≤ CTCAE Grade 2
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	96 (85.7)	206 (97.2)
Number of Subjects Censored, n (%)	16 (14.3)	6 (2.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.56 (0.33, 0.69)	0.26 (0.20, 0.36)
75% percentile (95% CI)	0.72 (0.69, 1.61)	0.69 (0.62, 0.69)
Min, Max	0.0, 4.7*	0.0, 3.7
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.519 (0.126)
95% CI		(1.186, 1.946)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
TEAE ≤ CTCAE Grade 2
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	12.3 (5.8, 18.7)	2.4 (0.1, 4.8)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.56	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
TEAE ≥ CTCAE Grade 3
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	49 (41.5)	148 (60.7)
Number of Subjects Censored, n (%)	69 (58.5)	96 (39.3)
Time to first TEAE (months)		
25% percentile (95% CI)	1.02 (0.72, 1.64)	0.95 (0.69, 1.28)
Median (95% CI)	NE (3.71, NE)	3.02 (2.00, 4.04)
75% percentile (95% CI)	NE (NE, NE)	11.04 (6.90, NE)
Min, Max	0.1, 6.8*	0.0, 16.1
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.336 (0.169)
95% CI		(0.960, 1.859)
Log-rank p-value		0.052

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
TEAE ≥ CTCAE Grade 3
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	60.3 (51.4, 69.3)	50.1 (43.7, 56.5)
6 months	50.3 (37.4, 63.1)	35.9 (28.9, 43.0)
9 months	NE (NE, NE)	27.5 (19.4, 35.6)
12 months	NE (NE, NE)	22.0 (10.4, 33.7)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.51	2.74

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
TEAE ≥ CTCAE Grade 3
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	54 (48.2)	129 (60.8)
Number of Subjects Censored, n (%)	58 (51.8)	83 (39.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.69, 1.41)	0.95 (0.69, 1.35)
Median (95% CI)	3.61 (2.00, 5.36)	2.79 (2.04, 3.98)
75% percentile (95% CI)	5.55 (4.83, NE)	9.20 (7.39, NE)
Min, Max	0.1, 9.3	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.101 (0.167)
95% CI		(0.794, 1.526)
Log-rank p-value		0.543

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
TEAE ≥ CTCAE Grade 3
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	58.0 (48.6, 67.3)	48.1 (41.2, 54.9)
6 months	18.4 (0.0, 38.5)	36.2 (28.5, 43.9)
9 months	18.4 (0.0, 38.5)	25.1 (15.3, 34.9)
12 months	0.0 (NE, NE)	16.9 (4.8, 29.1)
18 months	0.0 (NE, NE)	16.9 (4.8, 29.1)
Median Follow-up Time (months)	2.02	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
Discontinuation due to TEAE
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	18 (15.3)	42 (17.2)
Number of Subjects Censored, n (%)	100 (84.7)	202 (82.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	8.21 (6.28, NE)
Median (95% CI)	NE (NE, NE)	NE (11.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.698 (0.296)
95% CI		(0.391, 1.248)
Log-rank p-value		0.274

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
Discontinuation due to TEAE
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.9 (79.5, 92.3)	89.6 (85.7, 93.5)
6 months	76.9 (63.7, 90.1)	82.8 (77.2, 88.4)
9 months	NE (NE, NE)	72.5 (63.1, 81.8)
12 months	NE (NE, NE)	59.7 (40.9, 78.5)
18 months	NE (NE, NE)	59.7 (40.9, 78.5)
Median Follow-up Time (months)	2.83	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
Discontinuation due to TEAE
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	22 (19.6)	43 (20.3)
Number of Subjects Censored, n (%)	90 (80.4)	169 (79.7)
Time to first TEAE (months)		
25% percentile (95% CI)	3.98 (1.94, NE)	7.46 (4.37, NE)
Median (95% CI)	NE (4.83, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.695 (0.275)
95% CI		(0.406, 1.190)
Log-rank p-value		0.224

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
Discontinuation due to TEAE
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.2 (76.1, 90.3)	85.3 (80.4, 90.2)
6 months	59.7 (37.1, 82.2)	77.7 (71.0, 84.5)
9 months	59.7 (37.1, 82.2)	66.9 (56.1, 77.8)
12 months	59.7 (37.1, 82.2)	66.9 (56.1, 77.8)
18 months	NE (NE, NE)	66.9 (56.1, 77.8)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
Deaths (Grade 5 TEAEs)
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	5 (4.2)	11 (4.5)
Number of Subjects Censored, n (%)	113 (95.8)	233 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.616 (0.577)
95% CI		(0.199, 1.907)
Log-rank p-value		0.365

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
Deaths (Grade 5 TEAEs)
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (90.9, 99.3)	97.9 (96.1, 99.7)
6 months	95.1 (90.9, 99.3)	95.7 (92.6, 98.8)
9 months	NE (NE, NE)	91.9 (85.8, 98.1)
12 months	NE (NE, NE)	86.5 (74.7, 98.3)
18 months	NE (NE, NE)	86.5 (74.7, 98.3)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3B
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Age
Safety Population
Deaths (Grade 5 TEAEs)
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	11 (9.8)	8 (3.8)
Number of Subjects Censored, n (%)	101 (90.2)	204 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.98, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.275 (0.498)
95% CI		(0.104, 0.730)
Log-rank p-value		0.011

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
TEAE
Male

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.5 (83.3, 95.8)	97.4 (95.2, 99.7)
6 months	83.6 (70.8, 96.3)	95.2 (91.3, 99.0)
9 months	83.6 (70.8, 96.3)	93.6 (88.6, 98.5)
12 months	83.6 (70.8, 96.3)	93.6 (88.6, 98.5)
18 months	NE (NE, NE)	93.6 (88.6, 98.5)
Median Follow-up Time (months)	2.79	3.76

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	126 (90.0)	237 (98.3)
Number of Subjects Censored, n (%)	14 (10.0)	4 (1.7)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.20)	0.07 (0.07, 0.10)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
TEAE
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Median (95% CI)	0.46 (0.30, 0.66)	0.26 (0.20, 0.36)
75% percentile (95% CI)	0.72 (0.69, 1.28)	0.69 (0.62, 0.69)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.410 (0.113)
95% CI		(1.130, 1.760)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
TEAE
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	9.4 (4.5, 14.4)	2.1 (0.3, 3.9)
6 months	NE (NE, NE)	1.4 (0.0, 3.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
TEAE
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	85 (94.4)	213 (99.1)
Number of Subjects Censored, n (%)	5 (5.6)	2 (0.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.16 (0.07, 0.26)	0.07 (0.07, 0.10)
Median (95% CI)	0.51 (0.36, 0.66)	0.26 (0.20, 0.36)
75% percentile (95% CI)	0.69 (0.69, 0.92)	0.69 (0.59, 0.69)
Min, Max	0.0, 3.6	0.0, 5.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.358 (0.131)
95% CI		(1.050, 1.757)
Log-rank p-value		0.024

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
TEAE
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	6.7 (1.5, 11.8)	1.9 (0.1, 3.7)
6 months	0.0 (NE, NE)	0.0 (NE, NE)
9 months	0.0 (NE, NE)	0.0 (NE, NE)
12 months	0.0 (NE, NE)	0.0 (NE, NE)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.51	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
Serious TEAE
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	47 (33.6)	84 (34.9)
Number of Subjects Censored, n (%)	93 (66.4)	157 (65.1)
Time to first TEAE (months)		
25% percentile (95% CI)	1.28 (0.79, 2.40)	2.86 (1.84, 3.61)
Median (95% CI)	NE (4.14, NE)	9.23 (7.79, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.683 (0.190)
95% CI		(0.470, 0.992)
Log-rank p-value		0.039

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
Serious TEAE
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	67.4 (59.5, 75.4)	72.8 (67.0, 78.6)
6 months	55.6 (40.7, 70.5)	63.2 (56.3, 70.2)
9 months	55.6 (40.7, 70.5)	52.4 (42.0, 62.8)
12 months	55.6 (40.7, 70.5)	48.9 (37.1, 60.7)
18 months	NE (NE, NE)	48.9 (37.1, 60.7)
Median Follow-up Time (months)	2.66	3.48

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
Serious TEAE
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	25 (27.8)	70 (32.6)
Number of Subjects Censored, n (%)	65 (72.2)	145 (67.4)
Time to first TEAE (months)		
25% percentile (95% CI)	2.27 (1.31, NE)	3.19 (2.20, 4.83)
Median (95% CI)	NE (5.36, NE)	11.04 (7.75, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (11.96, NE)
Min, Max	0.2, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.845 (0.239)
95% CI		(0.529, 1.351)
Log-rank p-value		0.548

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
Serious TEAE
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.4 (64.0, 82.8)	75.8 (70.0, 81.7)
6 months	63.7 (48.2, 79.3)	63.5 (55.7, 71.3)
9 months	NE (NE, NE)	55.8 (45.6, 66.0)
12 months	NE (NE, NE)	35.9 (11.9, 59.8)
18 months	NE (NE, NE)	35.9 (11.9, 59.8)
Median Follow-up Time (months)	2.83	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
TEAE ≤ CTCAE Grade 2
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	119 (85.0)	233 (96.7)
Number of Subjects Censored, n (%)	21 (15.0)	8 (3.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.48 (0.36, 0.69)	0.26 (0.23, 0.39)
75% percentile (95% CI)	0.82 (0.69, 1.61)	0.69 (NE, NE)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.446 (0.116)
95% CI		(1.153, 1.814)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
TEAE ≤ CTCAE Grade 2
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	13.3 (7.4, 19.3)	2.7 (0.5, 4.9)
6 months	NE (NE, NE)	1.8 (0.0, 3.8)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.48	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
TEAE ≤ CTCAE Grade 2
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	81 (90.0)	211 (98.1)
Number of Subjects Censored, n (%)	9 (10.0)	4 (1.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.16 (0.07, 0.26)	0.10 (0.07, 0.13)
Median (95% CI)	0.59 (0.39, 0.69)	0.33 (0.23, 0.46)
75% percentile (95% CI)	0.72 (0.69, 1.02)	0.69 (NE, NE)
Min, Max	0.0, 4.7*	0.0, 5.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.387 (0.133)
95% CI		(1.068, 1.800)
Log-rank p-value		0.024

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
TEAE ≤ CTCAE Grade 2
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	8.3 (2.3, 14.3)	2.3 (0.2, 4.3)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.59	0.33

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
TEAE ≥ CTCAE Grade 3
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	59 (42.1)	139 (57.7)
Number of Subjects Censored, n (%)	81 (57.9)	102 (42.3)
Time to first TEAE (months)		
25% percentile (95% CI)	1.12 (0.72, 1.81)	1.15 (0.69, 1.41)
Median (95% CI)	3.71 (3.15, NE)	3.25 (2.66, 4.57)
75% percentile (95% CI)	9.26 (NE, NE)	16.07 (7.39, NE)
Min, Max	0.1, 9.3	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.143 (0.159)
95% CI		(0.837, 1.562)
Log-rank p-value		0.365

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
TEAE ≥ CTCAE Grade 3
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	61.1 (52.8, 69.3)	51.7 (45.3, 58.1)
6 months	43.7 (28.6, 58.7)	40.0 (33.1, 47.0)
9 months	43.7 (28.6, 58.7)	30.1 (20.6, 39.6)
12 months	0.0 (NE, NE)	25.8 (14.5, 37.0)
18 months	0.0 (NE, NE)	12.9 (0.0, 31.6)
Median Follow-up Time (months)	2.43	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
TEAE ≥ CTCAE Grade 3
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	44 (48.9)	138 (64.2)
Number of Subjects Censored, n (%)	46 (51.1)	77 (35.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.69, 1.41)	0.72 (0.66, 0.95)
Median (95% CI)	4.34 (1.87, NE)	2.56 (1.84, 3.91)
75% percentile (95% CI)	NE (5.36, NE)	8.38 (5.98, NE)
Min, Max	0.2, 6.8*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.254 (0.176)
95% CI		(0.887, 1.772)
Log-rank p-value		0.158

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
TEAE ≥ CTCAE Grade 3
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	56.2 (45.9, 66.6)	46.4 (39.6, 53.1)
6 months	34.5 (17.9, 51.1)	32.2 (24.7, 39.8)
9 months	NE (NE, NE)	22.6 (14.1, 31.2)
12 months	NE (NE, NE)	12.6 (0.6, 24.6)
18 months	NE (NE, NE)	12.6 (0.6, 24.6)
Median Follow-up Time (months)	2.25	2.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
Discontinuation due to TEAE
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	23 (16.4)	40 (16.6)
Number of Subjects Censored, n (%)	117 (83.6)	201 (83.4)
Time to first TEAE (months)		
25% percentile (95% CI)	4.57 (3.15, NE)	8.21 (6.18, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.3, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.654 (0.276)
95% CI		(0.381, 1.125)
Log-rank p-value		0.109

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
Discontinuation due to TEAE
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.0 (79.0, 91.1)	88.5 (84.4, 92.6)
6 months	71.0 (54.8, 87.1)	82.5 (76.8, 88.1)
9 months	71.0 (54.8, 87.1)	72.7 (63.1, 82.3)
12 months	71.0 (54.8, 87.1)	72.7 (63.1, 82.3)
18 months	NE (NE, NE)	72.7 (63.1, 82.3)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
Discontinuation due to TEAE
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	17 (18.9)	45 (20.9)
Number of Subjects Censored, n (%)	73 (81.1)	170 (79.1)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (2.10, NE)	7.46 (5.26, 9.69)
Median (95% CI)	NE (4.83, NE)	NE (9.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.691 (0.299)
95% CI		(0.385, 1.241)
Log-rank p-value		0.297

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
Discontinuation due to TEAE
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.8 (76.1, 91.6)	86.6 (82.0, 91.2)
6 months	66.9 (47.9, 85.9)	78.5 (71.9, 85.1)
9 months	NE (NE, NE)	67.0 (56.4, 77.6)
12 months	NE (NE, NE)	57.3 (41.7, 72.9)
18 months	NE (NE, NE)	57.3 (41.7, 72.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
Deaths (Grade 5 TEAEs)
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	11 (7.9)	8 (3.3)
Number of Subjects Censored, n (%)	129 (92.1)	233 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.98, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.239 (0.499)
95% CI		(0.090, 0.636)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
Deaths (Grade 5 TEAEs)
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.9 (87.1, 96.8)	98.3 (96.6, 100.0)
6 months	86.2 (74.4, 98.0)	94.8 (91.0, 98.6)
9 months	86.2 (74.4, 98.0)	94.8 (91.0, 98.6)
12 months	86.2 (74.4, 98.0)	94.8 (91.0, 98.6)
18 months	NE (NE, NE)	94.8 (91.0, 98.6)
Median Follow-up Time (months)	2.83	4.11

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3C
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Sex
Safety Population
Deaths (Grade 5 TEAEs)
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	5 (5.6)	11 (5.1)
Number of Subjects Censored, n (%)	85 (94.4)	204 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.524 (0.578)
95% CI		(0.169, 1.629)
Log-rank p-value		0.303

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
TEAE
North America

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.1 (87.3, 99.0)	97.1 (94.8, 99.4)
6 months	93.1 (87.3, 99.0)	96.1 (93.2, 99.1)
9 months	NE (NE, NE)	90.9 (84.4, 97.5)
12 months	NE (NE, NE)	85.9 (74.5, 97.3)
18 months	NE (NE, NE)	85.9 (74.5, 97.3)
Median Follow-up Time (months)	2.83	3.78

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	39 (95.1)	79 (98.8)
Number of Subjects Censored, n (%)	2 (4.9)	1 (1.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.20 (0.03, 0.43)	0.13 (0.07, 0.16)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
TEAE
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Median (95% CI)	0.49 (0.33, 0.69)	0.36 (0.23, 0.46)
75% percentile (95% CI)	0.72 (0.69, 1.02)	0.69 (0.46, 0.69)
Min, Max	0.0, 4.6*	0.0, 3.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.519 (0.203)
95% CI		(1.021, 2.259)
Log-rank p-value		0.043

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
TEAE
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	4.9 (0.0, 11.5)	1.2 (0.0, 3.7)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.49	0.36

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
TEAE
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	154 (92.2)	323 (98.8)
Number of Subjects Censored, n (%)	13 (7.8)	4 (1.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.10)	0.07 (NE, NE)
Median (95% CI)	0.46 (0.30, 0.59)	0.23 (0.20, 0.33)
75% percentile (95% CI)	0.69 (0.69, 0.82)	0.69 (NE, NE)
Min, Max	0.0, 3.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.309 (0.100)
95% CI		(1.077, 1.591)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
TEAE
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	7.9 (3.8, 12.1)	2.1 (0.6, 3.7)
6 months	NE (NE, NE)	0.9 (0.0, 2.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
TEAE
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	18 (81.8)	48 (98.0)
Number of Subjects Censored, n (%)	4 (18.2)	1 (2.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.33 (0.13, 0.39)	0.10 (0.07, 0.20)
Median (95% CI)	0.46 (0.33, 0.95)	0.26 (0.16, 0.30)
75% percentile (95% CI)	1.61 (0.46, NE)	0.46 (0.30, 0.69)
Min, Max	0.1, 2.8*	0.0, 3.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.320 (0.310)
95% CI		(1.263, 4.261)
Log-rank p-value		0.006

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
TEAE
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	NE (NE, NE)	2.0 (0.0, 6.0)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
Serious TEAE
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	12 (29.3)	34 (42.5)
Number of Subjects Censored, n (%)	29 (70.7)	46 (57.5)
Time to first TEAE (months)		
25% percentile (95% CI)	2.04 (0.89, NE)	1.87 (0.95, 3.25)
Median (95% CI)	NE (4.14, NE)	5.26 (3.29, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (7.79, NE)
Min, Max	0.3, 8.4*	0.1, 12.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.172 (0.350)
95% CI		(0.590, 2.325)
Log-rank p-value		0.401

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
Serious TEAE
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	69.7 (54.3, 85.1)	66.4 (55.5, 77.4)
6 months	58.1 (33.7, 82.5)	45.7 (31.2, 60.2)
9 months	NE (NE, NE)	38.1 (19.9, 56.3)
12 months	NE (NE, NE)	38.1 (19.9, 56.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.37	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
Serious TEAE
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	58 (34.7)	105 (32.1)
Number of Subjects Censored, n (%)	109 (65.3)	222 (67.9)
Time to first TEAE (months)		
25% percentile (95% CI)	1.28 (0.95, 2.27)	3.19 (2.40, 4.50)
Median (95% CI)	NE (5.36, NE)	11.96 (8.90, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.633 (0.169)
95% CI		(0.454, 0.882)
Log-rank p-value		0.010

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
Serious TEAE
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	66.8 (59.5, 74.1)	75.4 (70.6, 80.1)
6 months	56.1 (43.4, 68.8)	66.7 (60.9, 72.6)
9 months	56.1 (43.4, 68.8)	56.9 (48.4, 65.5)
12 months	56.1 (43.4, 68.8)	45.6 (31.7, 59.5)
18 months	NE (NE, NE)	45.6 (31.7, 59.5)
Median Follow-up Time (months)	2.79	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
Serious TEAE
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	2 (9.1)	15 (30.6)
Number of Subjects Censored, n (%)	20 (90.9)	34 (69.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.23, NE)	3.25 (1.58, NE)
Median (95% CI)	NE (NE, NE)	NE (4.90, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.5*	0.5, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.617 (0.793)
95% CI		(0.342, 7.645)
Log-rank p-value		0.637

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
Serious TEAE
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (78.9, 100.0)	78.9 (67.2, 90.6)
6 months	90.9 (78.9, 100.0)	65.7 (50.0, 81.4)
9 months	NE (NE, NE)	60.6 (43.3, 77.9)
12 months	NE (NE, NE)	60.6 (43.3, 77.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
TEAE ≤ CTCAE Grade 2
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	36 (87.8)	79 (98.8)
Number of Subjects Censored, n (%)	5 (12.2)	1 (1.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.20 (0.03, 0.46)	0.15 (0.10, 0.23)
Median (95% CI)	0.62 (0.39, 0.69)	0.39 (0.26, 0.46)
75% percentile (95% CI)	0.72 (0.69, 1.61)	0.69 (0.56, 0.69)
Min, Max	0.0, 4.6*	0.0, 3.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.576 (0.207)
95% CI		(1.051, 2.365)
Log-rank p-value		0.035

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
TEAE ≤ CTCAE Grade 2
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	11.4 (1.4, 21.4)	1.2 (0.0, 3.7)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.62	0.39

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
TEAE ≤ CTCAE Grade 2
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	146 (87.4)	318 (97.2)
Number of Subjects Censored, n (%)	21 (12.6)	9 (2.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.10)	0.07 (NE, NE)
Median (95% CI)	0.56 (0.30, 0.69)	0.26 (0.23, 0.39)
75% percentile (95% CI)	0.76 (0.69, 1.25)	0.69 (NE, NE)
Min, Max	0.0, 4.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.358 (0.101)
95% CI		(1.113, 1.657)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
TEAE ≤ CTCAE Grade 2
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	10.5 (5.6, 15.5)	2.7 (0.8, 4.6)
6 months	NE (NE, NE)	1.1 (0.0, 2.5)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.56	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
TEAE ≤ CTCAE Grade 2
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	18 (81.8)	47 (95.9)
Number of Subjects Censored, n (%)	4 (18.2)	2 (4.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.33 (0.13, 0.39)	0.13 (0.07, 0.23)
Median (95% CI)	0.46 (0.33, 0.95)	0.26 (0.23, 0.36)
75% percentile (95% CI)	1.61 (0.46, NE)	0.66 (0.36, 0.69)
Min, Max	0.1, 2.8*	0.0, 3.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.026 (0.312)
95% CI		(1.099, 3.735)
Log-rank p-value		0.031

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
TEAE ≤ CTCAE Grade 2
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	NE (NE, NE)	2.6 (0.0, 7.4)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	17 (41.5)	54 (67.5)
Number of Subjects Censored, n (%)	24 (58.5)	26 (32.5)
Time to first TEAE (months)		
25% percentile (95% CI)	1.35 (0.62, 2.04)	0.71 (0.53, 1.28)
Median (95% CI)	5.55 (2.00, NE)	1.87 (1.41, 3.35)
75% percentile (95% CI)	5.55 (NE, NE)	5.26 (3.61, NE)
Min, Max	0.3, 5.6	0.1, 12.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.619 (0.284)
95% CI		(0.928, 2.825)
Log-rank p-value		0.057

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	61.3 (45.7, 76.9)	41.7 (30.5, 52.9)
6 months	0.0 (NE, NE)	24.6 (13.1, 36.2)
9 months	0.0 (NE, NE)	18.5 (4.9, 32.0)
12 months	0.0 (NE, NE)	18.5 (4.9, 32.0)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.04	1.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	80 (47.9)	191 (58.4)
Number of Subjects Censored, n (%)	87 (52.1)	136 (41.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.72, 1.25)	1.12 (0.79, 1.35)
Median (95% CI)	3.65 (2.00, NE)	3.61 (2.60, 5.26)
75% percentile (95% CI)	9.26 (5.36, NE)	11.04 (7.46, NE)
Min, Max	0.1, 9.3	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.012 (0.136)
95% CI		(0.775, 1.322)
Log-rank p-value		0.814

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	56.2 (48.5, 63.8)	51.6 (46.1, 57.1)
6 months	37.8 (24.0, 51.6)	40.2 (34.0, 46.4)
9 months	37.8 (24.0, 51.6)	28.3 (20.5, 36.1)
12 months	0.0 (NE, NE)	18.7 (7.7, 29.6)
18 months	0.0 (NE, NE)	12.5 (0.1, 24.8)
Median Follow-up Time (months)	2.40	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	6 (27.3)	32 (65.3)
Number of Subjects Censored, n (%)	16 (72.7)	17 (34.7)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (0.23, NE)	0.69 (0.46, 1.54)
Median (95% CI)	4.34 (4.34, NE)	2.56 (1.18, 3.71)
75% percentile (95% CI)	NE (4.34, NE)	NE (3.25, NE)
Min, Max	0.2, 6.5*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.056 (0.459)
95% CI		(0.836, 5.059)
Log-rank p-value		0.152

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
TEAE ≥ CTCAE Grade 3
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.3 (59.8, 94.8)	44.9 (31.0, 58.8)
6 months	38.6 (0.0, 92.9)	26.1 (9.9, 42.4)
9 months	NE (NE, NE)	26.1 (9.9, 42.4)
12 months	NE (NE, NE)	26.1 (9.9, 42.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.32	2.56

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
Discontinuation due to TEAE
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	8 (19.5)	14 (17.5)
Number of Subjects Censored, n (%)	33 (80.5)	66 (82.5)
Time to first TEAE (months)		
25% percentile (95% CI)	4.57 (1.35, NE)	8.21 (4.11, NE)
Median (95% CI)	NE (4.57, NE)	NE (8.21, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 8.4*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.504 (0.467)
95% CI		(0.202, 1.258)
Log-rank p-value		0.205

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
Discontinuation due to TEAE
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.0 (69.9, 94.1)	91.0 (84.5, 97.4)
6 months	68.4 (41.9, 94.8)	82.7 (71.9, 93.5)
9 months	NE (NE, NE)	57.4 (34.7, 80.1)
12 months	NE (NE, NE)	57.4 (34.7, 80.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
Discontinuation due to TEAE
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	29 (17.4)	65 (19.9)
Number of Subjects Censored, n (%)	138 (82.6)	262 (80.1)
Time to first TEAE (months)		
25% percentile (95% CI)	4.83 (3.65, NE)	7.46 (5.39, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.781 (0.231)
95% CI		(0.496, 1.229)
Log-rank p-value		0.280

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
Discontinuation due to TEAE
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.4 (78.7, 90.0)	85.9 (82.1, 89.7)
6 months	71.4 (57.8, 85.0)	79.1 (73.9, 84.3)
9 months	71.4 (57.8, 85.0)	71.6 (64.0, 79.2)
12 months	71.4 (57.8, 85.0)	65.7 (55.2, 76.3)
18 months	NE (NE, NE)	65.7 (55.2, 76.3)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
Discontinuation due to TEAE
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	3 (13.6)	6 (12.2)
Number of Subjects Censored, n (%)	19 (86.4)	43 (87.8)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (0.23, NE)	8.28 (4.90, NE)
Median (95% CI)	4.34 (4.34, NE)	NE (8.28, NE)
75% percentile (95% CI)	NE (4.34, NE)	NE (NE, NE)
Min, Max	0.2, 6.5*	0.5, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.142 (0.948)
95% CI		(0.022, 0.909)
Log-rank p-value		0.028

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
Discontinuation due to TEAE
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (78.9, 100.0)	93.8 (87.1, 100.0)
6 months	45.5 (0.0, 100.0)	85.8 (73.1, 98.4)
9 months	NE (NE, NE)	71.5 (43.8, 99.1)
12 months	NE (NE, NE)	71.5 (43.8, 99.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
Deaths (Grade 5 TEAEs)
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	1 (2.4)	5 (6.3)
Number of Subjects Censored, n (%)	40 (97.6)	75 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.28, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 8.4*	0.8, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.018 (1.193)
95% CI		(0.098, 10.544)
Log-rank p-value		0.922

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
Deaths (Grade 5 TEAEs)
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (92.8, 100.0)	97.2 (93.4, 100.0)
6 months	97.6 (92.8, 100.0)	94.7 (88.5, 100.0)
9 months	NE (NE, NE)	82.3 (64.5, 100.0)
12 months	NE (NE, NE)	82.3 (64.5, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
Deaths (Grade 5 TEAEs)
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	15 (9.0)	13 (4.0)
Number of Subjects Censored, n (%)	152 (91.0)	314 (96.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.98, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.271 (0.403)
95% CI		(0.123, 0.596)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
Deaths (Grade 5 TEAEs)
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.3 (85.4, 95.2)	97.5 (95.8, 99.2)
6 months	86.5 (77.9, 95.1)	95.4 (92.5, 98.3)
9 months	86.5 (77.9, 95.1)	94.4 (91.0, 97.9)
12 months	86.5 (77.9, 95.1)	91.4 (84.6, 98.1)
18 months	NE (NE, NE)	91.4 (84.6, 98.1)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3D
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Geographic Region
Safety Population
Deaths (Grade 5 TEAEs)
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	1 (2.0)
Number of Subjects Censored, n (%)	22 (100.0)	48 (98.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.789

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
TEAE
ECOG: 0

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	100.0 (100.0, 100.0)	96.9 (90.8, 100.0)
9 months	NE (NE, NE)	96.9 (90.8, 100.0)
12 months	NE (NE, NE)	96.9 (90.8, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	90 (88.2)	189 (97.9)
Number of Subjects Censored, n (%)	12 (11.8)	4 (2.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.13 (0.07, 0.30)	0.10 (0.07, 0.13)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
TEAE
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Median (95% CI)	0.59 (0.46, 0.69)	0.26 (0.23, 0.36)
75% percentile (95% CI)	0.95 (0.69, 1.87)	0.69 (0.59, 0.69)
Min, Max	0.0, 3.6	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.740 (0.134)
95% CI		(1.340, 2.261)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
TEAE
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	12.5 (6.0, 18.9)	2.1 (0.1, 4.1)
6 months	0.0 (NE, NE)	2.1 (0.1, 4.1)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.59	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
TEAE
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	121 (94.5)	261 (99.2)
Number of Subjects Censored, n (%)	7 (5.5)	2 (0.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.20)	0.07 (NE, NE)
Median (95% CI)	0.39 (0.26, 0.53)	0.26 (0.20, 0.36)
75% percentile (95% CI)	0.69 (0.69, 0.76)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.6*	0.0, 5.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.222 (0.112)
95% CI		(0.980, 1.523)
Log-rank p-value		0.042

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
TEAE
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	5.0 (1.1, 8.9)	1.9 (0.3, 3.6)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.39	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
Serious TEAE
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	27 (26.5)	63 (32.6)
Number of Subjects Censored, n (%)	75 (73.5)	130 (67.4)
Time to first TEAE (months)		
25% percentile (95% CI)	3.35 (1.35, NE)	4.17 (2.96, 6.01)
Median (95% CI)	NE (4.14, NE)	11.96 (7.79, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (11.96, NE)
Min, Max	0.1, 8.4*	0.1, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.770 (0.243)
95% CI		(0.478, 1.239)
Log-rank p-value		0.397

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
Serious TEAE
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.1 (67.8, 84.5)	80.3 (74.6, 86.0)
6 months	65.0 (51.1, 78.9)	68.5 (61.0, 76.0)
9 months	NE (NE, NE)	54.6 (44.0, 65.2)
12 months	NE (NE, NE)	42.4 (24.2, 60.7)
18 months	NE (NE, NE)	42.4 (24.2, 60.7)
Median Follow-up Time (months)	2.83	4.44

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
Serious TEAE
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	45 (35.2)	91 (34.6)
Number of Subjects Censored, n (%)	83 (64.8)	172 (65.4)
Time to first TEAE (months)		
25% percentile (95% CI)	1.22 (0.76, 2.00)	2.20 (1.61, 2.86)
Median (95% CI)	NE (5.36, NE)	11.04 (8.90, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.735 (0.186)
95% CI		(0.510, 1.059)
Log-rank p-value		0.112

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
Serious TEAE
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	64.7 (56.0, 73.3)	69.6 (63.8, 75.4)
6 months	54.3 (37.8, 70.9)	59.1 (51.8, 66.4)
9 months	54.3 (37.8, 70.9)	56.2 (47.2, 65.1)
12 months	54.3 (37.8, 70.9)	49.9 (35.9, 63.9)
18 months	NE (NE, NE)	49.9 (35.9, 63.9)
Median Follow-up Time (months)	2.02	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
TEAE ≤ CTCAE Grade 2
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	86 (84.3)	188 (97.4)
Number of Subjects Censored, n (%)	16 (15.7)	5 (2.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.13 (0.07, 0.30)	0.10 (0.07, 0.13)
Median (95% CI)	0.66 (0.46, 0.69)	0.30 (0.23, 0.39)
75% percentile (95% CI)	1.02 (0.69, 1.87)	0.69 (NE, NE)
Min, Max	0.0, 4.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.699 (0.136)
95% CI		(1.303, 2.217)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
TEAE ≤ CTCAE Grade 2
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	14.5 (7.5, 21.6)	2.3 (0.1, 4.5)
6 months	NE (NE, NE)	2.3 (0.1, 4.5)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.66	0.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
TEAE ≤ CTCAE Grade 2
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	114 (89.1)	256 (97.3)
Number of Subjects Censored, n (%)	14 (10.9)	7 (2.7)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.30, 0.62)	0.30 (0.23, 0.46)
75% percentile (95% CI)	0.72 (0.69, 1.02)	0.69 (NE, NE)
Min, Max	0.0, 4.6*	0.0, 5.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.290 (0.115)
95% CI		(1.029, 1.616)
Log-rank p-value		0.015

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
TEAE ≤ CTCAE Grade 2
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	8.6 (3.2, 13.9)	2.7 (0.6, 4.8)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.46	0.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
TEAE ≥ CTCAE Grade 3
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	33 (32.4)	118 (61.1)
Number of Subjects Censored, n (%)	69 (67.6)	75 (38.9)
Time to first TEAE (months)		
25% percentile (95% CI)	2.27 (1.02, 4.14)	1.18 (0.69, 1.51)
Median (95% CI)	5.55 (4.14, NE)	3.71 (2.69, 5.19)
75% percentile (95% CI)	NE (5.55, NE)	9.20 (7.10, NE)
Min, Max	0.1, 6.5*	0.0, 16.1
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.663 (0.202)
95% CI		(1.119, 2.472)
Log-rank p-value		0.009

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
TEAE ≥ CTCAE Grade 3
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.3 (64.7, 81.9)	54.4 (47.3, 61.5)
6 months	40.1 (16.8, 63.3)	38.5 (30.7, 46.4)
9 months	NE (NE, NE)	25.5 (16.5, 34.6)
12 months	NE (NE, NE)	14.6 (1.1, 28.1)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
TEAE ≥ CTCAE Grade 3
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	70 (54.7)	159 (60.5)
Number of Subjects Censored, n (%)	58 (45.3)	104 (39.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.72 (0.69, 0.99)	0.92 (0.69, 1.15)
Median (95% CI)	2.00 (1.35, 5.36)	2.53 (1.87, 3.35)
75% percentile (95% CI)	9.26 (5.36, NE)	11.04 (8.38, NE)
Min, Max	0.1, 9.3	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.939 (0.146)
95% CI		(0.705, 1.249)
Log-rank p-value		0.819

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
TEAE ≥ CTCAE Grade 3
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	47.6 (38.7, 56.5)	45.3 (39.2, 51.5)
6 months	32.9 (17.8, 47.9)	34.9 (28.0, 41.8)
9 months	32.9 (17.8, 47.9)	28.3 (19.2, 37.4)
12 months	0.0 (NE, NE)	24.3 (13.6, 35.0)
18 months	0.0 (NE, NE)	24.3 (13.6, 35.0)
Median Follow-up Time (months)	1.87	2.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
Discontinuation due to TEAE
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	14 (13.7)	30 (15.5)
Number of Subjects Censored, n (%)	88 (86.3)	163 (84.5)
Time to first TEAE (months)		
25% percentile (95% CI)	4.83 (3.65, NE)	8.28 (6.28, NE)
Median (95% CI)	NE (4.83, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.573 (0.352)
95% CI		(0.288, 1.142)
Log-rank p-value		0.181

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
Discontinuation due to TEAE
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (84.1, 95.9)	92.7 (89.0, 96.4)
6 months	67.8 (47.6, 88.0)	85.1 (79.1, 91.0)
9 months	NE (NE, NE)	73.9 (64.5, 83.3)
12 months	NE (NE, NE)	73.9 (64.5, 83.3)
18 months	NE (NE, NE)	73.9 (64.5, 83.3)
Median Follow-up Time (months)	2.83	4.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
Discontinuation due to TEAE
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	26 (20.3)	55 (20.9)
Number of Subjects Censored, n (%)	102 (79.7)	208 (79.1)
Time to first TEAE (months)		
25% percentile (95% CI)	3.98 (1.77, NE)	8.21 (4.07, 9.69)
Median (95% CI)	NE (NE, NE)	NE (9.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.726 (0.245)
95% CI		(0.449, 1.174)
Log-rank p-value		0.210

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
Discontinuation due to TEAE
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.0 (72.7, 87.2)	83.8 (79.2, 88.4)
6 months	71.1 (57.2, 85.0)	77.0 (70.8, 83.2)
9 months	71.1 (57.2, 85.0)	67.0 (56.3, 77.7)
12 months	71.1 (57.2, 85.0)	57.8 (42.6, 73.0)
18 months	NE (NE, NE)	57.8 (42.6, 73.0)
Median Follow-up Time (months)	2.51	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
Deaths (Grade 5 TEAEs)
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	5 (4.9)	6 (3.1)
Number of Subjects Censored, n (%)	97 (95.1)	187 (96.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 8.4*	0.8, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.344 (0.650)
95% CI		(0.096, 1.230)
Log-rank p-value		0.109

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
Deaths (Grade 5 TEAEs)
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.7 (90.2, 99.2)	99.0 (97.5, 100.0)
6 months	94.7 (90.2, 99.2)	97.4 (94.9, 100.0)
9 months	NE (NE, NE)	94.8 (90.5, 99.2)
12 months	NE (NE, NE)	94.8 (90.5, 99.2)
18 months	NE (NE, NE)	94.8 (90.5, 99.2)
Median Follow-up Time (months)	2.83	4.93

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3E
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by ECOG PS
Safety Population
Deaths (Grade 5 TEAEs)
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	11 (8.6)	13 (4.9)
Number of Subjects Censored, n (%)	117 (91.4)	250 (95.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.98, NE)	NE (9.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.351 (0.438)
95% CI		(0.149, 0.829)
Log-rank p-value		0.014

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
TEAE
<= 18 months

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.3 (84.5, 96.1)	96.7 (94.5, 99.0)
6 months	83.9 (70.5, 97.2)	93.6 (89.5, 97.8)
9 months	83.9 (70.5, 97.2)	90.9 (84.2, 97.5)
12 months	83.9 (70.5, 97.2)	85.8 (74.3, 97.3)
18 months	NE (NE, NE)	85.8 (74.3, 97.3)
Median Follow-up Time (months)	2.58	3.25

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	12 (92.3)	35 (94.6)
Number of Subjects Censored, n (%)	1 (7.7)	2 (5.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.13 (0.03, 0.30)	0.23 (0.03, 0.26)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
TEAE
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Median (95% CI)	0.30 (0.10, 0.69)	0.39 (0.26, 0.69)
75% percentile (95% CI)	0.69 (0.26, NE)	0.69 (0.56, 0.72)
Min, Max	0.0, 3.7*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.000 (0.358)
95% CI		(0.496, 2.016)
Log-rank p-value		0.875

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
TEAE
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	7.7 (0.0, 22.2)	5.4 (0.0, 12.7)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.30	0.39

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
TEAE
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	199 (91.7)	415 (99.0)
Number of Subjects Censored, n (%)	18 (8.3)	4 (1.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.39, 0.59)	0.26 (0.20, 0.30)
75% percentile (95% CI)	0.72 (0.69, 0.82)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.429 (0.088)
95% CI		(1.203, 1.697)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
TEAE
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	8.4 (4.6, 12.1)	1.6 (0.4, 2.9)
6 months	NE (NE, NE)	0.4 (0.0, 1.2)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
Serious TEAE
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	7 (53.8)	6 (16.2)
Number of Subjects Censored, n (%)	6 (46.2)	31 (83.8)
Time to first TEAE (months)		
25% percentile (95% CI)	1.94 (0.23, 2.30)	NE (1.45, NE)
Median (95% CI)	2.30 (0.72, NE)	NE (NE, NE)
75% percentile (95% CI)	4.14 (2.00, NE)	NE (NE, NE)
Min, Max	0.2, 4.1	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.229 (0.577)
95% CI		(0.074, 0.710)
Log-rank p-value		0.018

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
Serious TEAE
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	44.0 (12.9, 75.0)	83.8 (71.9, 95.7)
6 months	0.0 (NE, NE)	83.8 (71.9, 95.7)
9 months	0.0 (NE, NE)	83.8 (71.9, 95.7)
12 months	0.0 (NE, NE)	83.8 (71.9, 95.7)
18 months	0.0 (NE, NE)	83.8 (71.9, 95.7)
Median Follow-up Time (months)	1.94	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
Serious TEAE
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	65 (30.0)	148 (35.3)
Number of Subjects Censored, n (%)	152 (70.0)	271 (64.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.58 (1.15, 3.35)	2.86 (2.17, 3.48)
Median (95% CI)	NE (5.36, NE)	11.04 (7.79, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.817 (0.154)
95% CI		(0.605, 1.105)
Log-rank p-value		0.230

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
Serious TEAE
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.0 (64.9, 77.2)	73.4 (69.1, 77.8)
6 months	61.7 (50.5, 72.8)	62.0 (56.5, 67.4)
9 months	61.7 (50.5, 72.8)	52.8 (45.4, 60.2)
12 months	61.7 (50.5, 72.8)	43.5 (31.6, 55.4)
18 months	NE (NE, NE)	43.5 (31.6, 55.4)
Median Follow-up Time (months)	2.79	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
TEAE ≤ CTCAE Grade 2
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	11 (84.6)	34 (91.9)
Number of Subjects Censored, n (%)	2 (15.4)	3 (8.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.13 (0.03, 0.30)	0.23 (0.03, 0.33)
Median (95% CI)	0.30 (0.10, 0.69)	0.46 (0.26, 0.69)
75% percentile (95% CI)	0.69 (0.30, NE)	0.69 (0.66, 1.61)
Min, Max	0.0, 3.7*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.958 (0.369)
95% CI		(0.465, 1.973)
Log-rank p-value		0.706

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
TEAE ≤ CTCAE Grade 2
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	15.4 (0.0, 35.0)	6.8 (0.0, 15.4)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.30	0.46

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
TEAE ≤ CTCAE Grade 2
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	189 (87.1)	410 (97.9)
Number of Subjects Censored, n (%)	28 (12.9)	9 (2.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.56 (0.46, 0.69)	0.26 (0.23, 0.39)
75% percentile (95% CI)	0.76 (0.69, 1.25)	0.69 (NE, NE)
Min, Max	0.0, 4.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.468 (0.090)
95% CI		(1.232, 1.750)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
TEAE ≤ CTCAE Grade 2
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	11.1 (6.6, 15.5)	2.0 (0.6, 3.5)
6 months	NE (NE, NE)	0.5 (0.0, 1.4)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.56	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
TEAE ≥ CTCAE Grade 3
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	7 (53.8)	12 (32.4)
Number of Subjects Censored, n (%)	6 (46.2)	25 (67.6)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.23, 2.00)	1.51 (0.69, NE)
Median (95% CI)	2.00 (0.72, NE)	NE (NE, NE)
75% percentile (95% CI)	4.14 (1.94, NE)	NE (NE, NE)
Min, Max	0.2, 4.1	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.544 (0.500)
95% CI		(0.204, 1.449)
Log-rank p-value		0.380

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
TEAE ≥ CTCAE Grade 3
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	46.2 (15.1, 77.2)	67.6 (52.5, 82.7)
6 months	0.0 (NE, NE)	67.6 (52.5, 82.7)
9 months	0.0 (NE, NE)	67.6 (52.5, 82.7)
12 months	0.0 (NE, NE)	67.6 (52.5, 82.7)
18 months	0.0 (NE, NE)	67.6 (52.5, 82.7)
Median Follow-up Time (months)	1.91	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
TEAE ≥ CTCAE Grade 3
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	96 (44.2)	265 (63.2)
Number of Subjects Censored, n (%)	121 (55.8)	154 (36.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.99 (0.76, 1.28)	0.92 (0.69, 1.15)
Median (95% CI)	4.34 (3.35, NE)	2.79 (2.23, 3.52)
75% percentile (95% CI)	9.26 (5.55, NE)	8.90 (7.33, NE)
Min, Max	0.1, 9.3	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.273 (0.122)
95% CI		(1.002, 1.617)
Log-rank p-value		0.034

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
TEAE ≥ CTCAE Grade 3
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	59.7 (53.1, 66.3)	47.6 (42.7, 52.4)
6 months	37.3 (23.5, 51.1)	34.3 (29.0, 39.5)
9 months	37.3 (23.5, 51.1)	24.0 (17.4, 30.5)
12 months	0.0 (NE, NE)	16.8 (8.2, 25.4)
18 months	0.0 (NE, NE)	8.4 (0.0, 20.8)
Median Follow-up Time (months)	2.40	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
Discontinuation due to TEAE
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	3 (23.1)	3 (8.1)
Number of Subjects Censored, n (%)	10 (76.9)	34 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	4.57 (0.23, NE)	NE (NE, NE)
Median (95% CI)	4.57 (1.94, NE)	NE (NE, NE)
75% percentile (95% CI)	4.57 (NE, NE)	NE (NE, NE)
Min, Max	0.2, 4.6	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.282 (0.852)
95% CI		(0.053, 1.494)
Log-rank p-value		0.164

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
Discontinuation due to TEAE
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.1 (52.2, 100.0)	91.9 (83.1, 100.0)
6 months	0.0 (NE, NE)	91.9 (83.1, 100.0)
9 months	0.0 (NE, NE)	91.9 (83.1, 100.0)
12 months	0.0 (NE, NE)	91.9 (83.1, 100.0)
18 months	0.0 (NE, NE)	91.9 (83.1, 100.0)
Median Follow-up Time (months)	1.94	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
Discontinuation due to TEAE
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	37 (17.1)	82 (19.6)
Number of Subjects Censored, n (%)	180 (82.9)	337 (80.4)
Time to first TEAE (months)		
25% percentile (95% CI)	4.83 (3.65, NE)	7.52 (5.72, 9.69)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.711 (0.208)
95% CI		(0.474, 1.069)
Log-rank p-value		0.123

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
Discontinuation due to TEAE
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.7 (79.8, 89.6)	87.3 (84.0, 90.5)
6 months	71.3 (59.1, 83.6)	79.9 (75.3, 84.4)
9 months	71.3 (59.1, 83.6)	68.9 (61.5, 76.3)
12 months	71.3 (59.1, 83.6)	63.8 (54.1, 73.6)
18 months	NE (NE, NE)	63.8 (54.1, 73.6)
Median Follow-up Time (months)	2.83	3.98

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
Deaths (Grade 5 TEAEs)
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	2 (15.4)	0
Number of Subjects Censored, n (%)	11 (84.6)	37 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	2.46 (2.30, NE)	NE (NE, NE)
Median (95% CI)	NE (2.30, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	1.1*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.007

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
Deaths (Grade 5 TEAEs)
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.4 (38.0, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3F
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Duration of Metastatic Disease
Safety Population
Deaths (Grade 5 TEAEs)
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	14 (6.5)	19 (4.5)
Number of Subjects Censored, n (%)	203 (93.5)	400 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.400 (0.377)
95% CI		(0.191, 0.837)
Log-rank p-value		0.014

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE
Colon

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.3 (89.7, 96.8)	97.5 (96.0, 99.0)
6 months	90.5 (84.0, 96.9)	95.2 (92.6, 97.7)
9 months	90.5 (84.0, 96.9)	92.4 (88.4, 96.5)
12 months	90.5 (84.0, 96.9)	89.9 (83.5, 96.2)
18 months	NE (NE, NE)	89.9 (83.5, 96.2)
Median Follow-up Time (months)	2.83	4.24

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	128 (92.8)	272 (98.6)
Number of Subjects Censored, n (%)	10 (7.2)	4 (1.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.13 (0.07, 0.23)	0.10 (0.07, 0.10)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Median (95% CI)	0.46 (0.33, 0.59)	0.28 (0.23, 0.39)
75% percentile (95% CI)	0.69 (0.69, 0.76)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.298 (0.109)
95% CI		(1.048, 1.607)
Log-rank p-value		0.017

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	7.4 (2.9, 11.9)	2.5 (0.6, 4.3)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.28

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	62 (89.9)	139 (98.6)
Number of Subjects Censored, n (%)	7 (10.1)	2 (1.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.23)	0.07 (0.07, 0.10)
Median (95% CI)	0.59 (0.26, 0.69)	0.26 (0.20, 0.36)
75% percentile (95% CI)	0.76 (0.69, 1.87)	0.69 (0.56, 0.69)
Min, Max	0.0, 3.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.499 (0.162)
95% CI		(1.091, 2.061)
Log-rank p-value		0.014

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	10.1 (3.0, 17.3)	1.4 (0.0, 3.4)
6 months	NE (NE, NE)	1.4 (0.0, 3.4)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.59	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	21 (91.3)	39 (100.0)
Number of Subjects Censored, n (%)	2 (8.7)	0
Time to first TEAE (months)		
25% percentile (95% CI)	0.03 (0.03, 0.36)	0.07 (0.03, 0.07)
Median (95% CI)	0.46 (0.07, 0.72)	0.13 (0.07, 0.39)
75% percentile (95% CI)	0.82 (0.46, 1.94)	0.66 (0.20, NE)
Min, Max	0.0, 2.9*	0.0, 0.7
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.141 (0.312)
95% CI		(1.161, 3.946)
Log-rank p-value		0.020

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	NE (NE, NE)	0.0 (NE, NE)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.46	0.13

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	41 (29.7)	95 (34.4)
Number of Subjects Censored, n (%)	97 (70.3)	181 (65.6)
Time to first TEAE (months)		
25% percentile (95% CI)	2.00 (1.12, 5.36)	2.86 (1.87, 3.81)
Median (95% CI)	NE (5.36, NE)	9.23 (7.03, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (11.96, NE)
Min, Max	0.2, 6.5*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.825 (0.195)
95% CI		(0.563, 1.210)
Log-rank p-value		0.301

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	70.5 (62.6, 78.3)	73.6 (68.3, 79.0)
6 months	55.0 (33.3, 76.8)	61.9 (55.0, 68.9)
9 months	NE (NE, NE)	53.0 (43.2, 62.8)
12 months	NE (NE, NE)	34.2 (14.5, 53.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.61	3.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	25 (36.2)	49 (34.8)
Number of Subjects Censored, n (%)	44 (63.8)	92 (65.2)
Time to first TEAE (months)		
25% percentile (95% CI)	1.28 (0.92, 3.15)	2.96 (1.87, 4.90)
Median (95% CI)	NE (3.15, NE)	18.04 (7.79, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.1, 13.0*	0.1, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.606 (0.257)
95% CI		(0.366, 1.003)
Log-rank p-value		0.097

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	66.7 (55.2, 78.1)	74.9 (67.6, 82.2)
6 months	53.9 (37.3, 70.5)	63.6 (54.5, 72.7)
9 months	53.9 (37.3, 70.5)	53.0 (40.8, 65.1)
12 months	53.9 (37.3, 70.5)	53.0 (40.8, 65.1)
18 months	NE (NE, NE)	53.0 (40.8, 65.1)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	6 (26.1)	10 (25.6)
Number of Subjects Censored, n (%)	17 (73.9)	29 (74.4)
Time to first TEAE (months)		
25% percentile (95% CI)	2.00 (0.16, NE)	4.07 (0.92, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.925 (0.534)
95% CI		(0.325, 2.632)
Log-rank p-value		0.846

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
Serious TEAE
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.7 (55.5, 91.8)	76.4 (62.8, 89.9)
6 months	73.7 (55.5, 91.8)	71.3 (55.4, 87.2)
9 months	NE (NE, NE)	71.3 (55.4, 87.2)
12 months	NE (NE, NE)	71.3 (55.4, 87.2)
18 months	NE (NE, NE)	71.3 (55.4, 87.2)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≤ CTCAE Grade 2
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	119 (86.2)	268 (97.1)
Number of Subjects Censored, n (%)	19 (13.8)	8 (2.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.13 (0.07, 0.23)	0.10 (0.07, 0.10)
Median (95% CI)	0.51 (0.39, 0.69)	0.36 (0.26, 0.46)
75% percentile (95% CI)	0.72 (0.69, 1.02)	0.69 (0.69, 0.72)
Min, Max	0.0, 4.7*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.366 (0.112)
95% CI		(1.097, 1.700)
Log-rank p-value		0.009

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≤ CTCAE Grade 2
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	12.4 (6.5, 18.2)	3.1 (0.9, 5.3)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.51	0.36

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≤ CTCAE Grade 2
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	60 (87.0)	137 (97.2)
Number of Subjects Censored, n (%)	9 (13.0)	4 (2.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.23)	0.10 (0.07, 0.13)
Median (95% CI)	0.59 (0.30, 0.69)	0.26 (0.23, 0.39)
75% percentile (95% CI)	0.95 (0.69, 1.87)	0.69 (0.66, 0.69)
Min, Max	0.0, 3.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.461 (0.163)
95% CI		(1.060, 2.012)
Log-rank p-value		0.022

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≤ CTCAE Grade 2
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	11.3 (3.6, 19.0)	1.7 (0.0, 3.9)
6 months	NE (NE, NE)	1.7 (0.0, 3.9)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.59	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≤ CTCAE Grade 2
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	21 (91.3)	39 (100.0)
Number of Subjects Censored, n (%)	2 (8.7)	0
Time to first TEAE (months)		
25% percentile (95% CI)	0.03 (0.03, 0.36)	0.07 (0.03, 0.07)
Median (95% CI)	0.46 (0.07, 0.72)	0.13 (0.07, 0.39)
75% percentile (95% CI)	0.82 (0.46, 1.94)	0.66 (0.20, NE)
Min, Max	0.0, 2.9*	0.0, 0.7
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.141 (0.312)
95% CI		(1.161, 3.946)
Log-rank p-value		0.020

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≤ CTCAE Grade 2
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	NE (NE, NE)	0.0 (NE, NE)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.46	0.13

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≥ CTCAE Grade 3
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	56 (40.6)	169 (61.2)
Number of Subjects Censored, n (%)	82 (59.4)	107 (38.8)
Time to first TEAE (months)		
25% percentile (95% CI)	1.15 (0.72, 1.81)	0.89 (0.69, 1.25)
Median (95% CI)	5.36 (3.61, NE)	2.83 (1.91, 4.04)
75% percentile (95% CI)	NE (NE, NE)	8.90 (6.90, NE)
Min, Max	0.2, 6.5*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.395 (0.158)
95% CI		(1.023, 1.903)
Log-rank p-value		0.039

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≥ CTCAE Grade 3
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	60.8 (52.5, 69.1)	49.0 (43.0, 55.0)
6 months	44.7 (25.9, 63.5)	35.9 (29.1, 42.6)
9 months	NE (NE, NE)	25.0 (16.4, 33.6)
12 months	NE (NE, NE)	12.0 (0.0, 23.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.37	2.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≥ CTCAE Grade 3
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	35 (50.7)	86 (61.0)
Number of Subjects Censored, n (%)	34 (49.3)	55 (39.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.69, 1.28)	1.15 (0.69, 1.51)
Median (95% CI)	3.71 (1.38, 4.83)	3.25 (2.37, 4.70)
75% percentile (95% CI)	9.26 (4.14, NE)	16.07 (7.10, NE)
Min, Max	0.1, 9.3	0.1, 16.1
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.961 (0.210)
95% CI		(0.636, 1.450)
Log-rank p-value		0.863

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≥ CTCAE Grade 3
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	58.5 (46.7, 70.3)	50.7 (42.3, 59.1)
6 months	28.4 (9.3, 47.6)	35.9 (26.7, 45.1)
9 months	28.4 (9.3, 47.6)	25.8 (15.0, 36.6)
12 months	0.0 (NE, NE)	25.8 (15.0, 36.6)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.27	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≥ CTCAE Grade 3
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	12 (52.2)	22 (56.4)
Number of Subjects Censored, n (%)	11 (47.8)	17 (43.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.62 (0.16, 1.87)	0.69 (0.53, 1.31)
Median (95% CI)	5.55 (1.61, NE)	2.53 (1.15, NE)
75% percentile (95% CI)	NE (5.55, NE)	NE (3.19, NE)
Min, Max	0.2, 6.8*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.162 (0.378)
95% CI		(0.554, 2.438)
Log-rank p-value		0.730

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE ≥ CTCAE Grade 3
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	51.8 (31.2, 72.4)	45.0 (29.1, 60.9)
6 months	25.9 (0.0, 63.3)	40.0 (23.1, 56.9)
9 months	NE (NE, NE)	40.0 (23.1, 56.9)
12 months	NE (NE, NE)	40.0 (23.1, 56.9)
18 months	NE (NE, NE)	40.0 (23.1, 56.9)
Median Follow-up Time (months)	2.00	1.91

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
Discontinuation due to TEAE
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	24 (17.4)	58 (21.0)
Number of Subjects Censored, n (%)	114 (82.6)	218 (79.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.65, NE)	6.90 (4.76, 8.90)
Median (95% CI)	NE (NE, NE)	NE (9.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.763 (0.257)
95% CI		(0.461, 1.263)
Log-rank p-value		0.266

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
Discontinuation due to TEAE
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.9 (76.5, 89.3)	87.4 (83.4, 91.3)
6 months	78.5 (68.3, 88.8)	76.4 (70.1, 82.8)
9 months	NE (NE, NE)	63.5 (52.9, 74.2)
12 months	NE (NE, NE)	53.8 (38.1, 69.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
Discontinuation due to TEAE
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	13 (18.8)	21 (14.9)
Number of Subjects Censored, n (%)	56 (81.2)	120 (85.1)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (3.15, 4.83)	NE (7.46, NE)
Median (95% CI)	NE (4.34, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.497 (0.377)
95% CI		(0.237, 1.042)
Log-rank p-value		0.121

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
Discontinuation due to TEAE
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.2 (78.9, 95.6)	89.0 (83.7, 94.3)
6 months	52.6 (27.2, 77.9)	86.5 (80.4, 92.7)
9 months	52.6 (27.2, 77.9)	76.9 (66.3, 87.5)
12 months	52.6 (27.2, 77.9)	76.9 (66.3, 87.5)
18 months	NE (NE, NE)	76.9 (66.3, 87.5)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
Discontinuation due to TEAE
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	3 (13.0)	6 (15.4)
Number of Subjects Censored, n (%)	20 (87.0)	33 (84.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.23, NE)	NE (0.89, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.080 (0.731)
95% CI		(0.258, 4.523)
Log-rank p-value		0.896

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
Discontinuation due to TEAE
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.0 (73.2, 100.0)	84.6 (73.3, 95.9)
6 months	87.0 (73.2, 100.0)	84.6 (73.3, 95.9)
9 months	NE (NE, NE)	84.6 (73.3, 95.9)
12 months	NE (NE, NE)	84.6 (73.3, 95.9)
18 months	NE (NE, NE)	84.6 (73.3, 95.9)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
Deaths (Grade 5 TEAEs)
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	11 (8.0)	14 (5.1)
Number of Subjects Censored, n (%)	127 (92.0)	262 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 6.8*	0.8, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.377 (0.438)
95% CI		(0.160, 0.891)
Log-rank p-value		0.029

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
Deaths (Grade 5 TEAEs)
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (85.7, 96.1)	97.3 (95.4, 99.3)
6 months	90.9 (85.7, 96.1)	93.9 (90.1, 97.8)
9 months	NE (NE, NE)	91.3 (86.2, 96.5)
12 months	NE (NE, NE)	86.3 (75.4, 97.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
Deaths (Grade 5 TEAEs)
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	4 (5.8)	4 (2.8)
Number of Subjects Censored, n (%)	65 (94.2)	137 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.98, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.295 (0.769)
95% CI		(0.065, 1.332)
Log-rank p-value		0.111

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
Deaths (Grade 5 TEAEs)
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (89.1, 100.0)	98.6 (96.6, 100.0)
6 months	87.6 (72.9, 100.0)	97.6 (94.8, 100.0)
9 months	87.6 (72.9, 100.0)	94.5 (88.0, 100.0)
12 months	87.6 (72.9, 100.0)	94.5 (88.0, 100.0)
18 months	NE (NE, NE)	94.5 (88.0, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3G
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Primary Tumor Site at 1st Diagnosis
Safety Population
Deaths (Grade 5 TEAEs)
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	1 (4.3)	1 (2.6)
Number of Subjects Censored, n (%)	22 (95.7)	38 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.20, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.9, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.667 (1.517)
95% CI		(0.034, 13.045)
Log-rank p-value		0.903

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (83.9, 100.0)	97.4 (92.5, 100.0)
6 months	94.4 (83.9, 100.0)	97.4 (92.5, 100.0)
9 months	NE (NE, NE)	97.4 (92.5, 100.0)
12 months	NE (NE, NE)	97.4 (92.5, 100.0)
18 months	NE (NE, NE)	97.4 (92.5, 100.0)
Median Follow-up Time (months)	2.83	3.02

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	81 (95.3)	167 (98.8)
Number of Subjects Censored, n (%)	4 (4.7)	2 (1.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.13)	0.07 (0.07, 0.10)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Median (95% CI)	0.39 (0.20, 0.59)	0.23 (0.16, 0.36)
75% percentile (95% CI)	0.69 (0.66, 0.76)	0.69 (0.62, 0.69)
Min, Max	0.0, 3.6	0.0, 5.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.184 (0.137)
95% CI		(0.905, 1.548)
Log-rank p-value		0.239

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	5.9 (0.9, 10.9)	2.4 (0.1, 4.7)
6 months	0.0 (NE, NE)	0.0 (NE, NE)
9 months	0.0 (NE, NE)	0.0 (NE, NE)
12 months	0.0 (NE, NE)	0.0 (NE, NE)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.39	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
TEAE
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	130 (89.7)	283 (98.6)
Number of Subjects Censored, n (%)	15 (10.3)	4 (1.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.16 (0.07, 0.26)	0.07 (0.07, 0.10)
Median (95% CI)	0.56 (0.39, 0.69)	0.26 (0.23, 0.36)
75% percentile (95% CI)	0.72 (0.69, 1.28)	0.69 (0.62, 0.69)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.580 (0.108)
95% CI		(1.277, 1.954)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
TEAE
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	9.8 (4.9, 14.8)	1.7 (0.2, 3.2)
6 months	NE (NE, NE)	1.1 (0.0, 2.5)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.56	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
Serious TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	25 (29.4)	57 (33.7)
Number of Subjects Censored, n (%)	60 (70.6)	112 (66.3)
Time to first TEAE (months)		
25% percentile (95% CI)	2.40 (0.99, 4.14)	2.96 (1.77, 4.80)
Median (95% CI)	NE (3.65, NE)	11.96 (7.75, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (11.96, NE)
Min, Max	0.2, 6.8*	0.1, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.812 (0.248)
95% CI		(0.500, 1.319)
Log-rank p-value		0.540

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
Serious TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	74.0 (64.4, 83.7)	74.9 (68.2, 81.6)
6 months	56.5 (39.1, 74.0)	63.5 (55.0, 72.0)
9 months	NE (NE, NE)	56.3 (45.6, 67.1)
12 months	NE (NE, NE)	38.0 (14.0, 62.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
Serious TEAE
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	47 (32.4)	97 (33.8)
Number of Subjects Censored, n (%)	98 (67.6)	190 (66.2)
Time to first TEAE (months)		
25% percentile (95% CI)	1.35 (0.89, 2.33)	2.86 (1.87, 3.81)
Median (95% CI)	NE (5.36, NE)	11.04 (7.82, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.774 (0.184)
95% CI		(0.540, 1.110)
Log-rank p-value		0.171

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
Serious TEAE
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	67.3 (59.5, 75.1)	73.9 (68.6, 79.1)
6 months	59.8 (44.3, 75.3)	63.1 (56.4, 69.7)
9 months	59.8 (44.3, 75.3)	53.2 (43.9, 62.6)
12 months	59.8 (44.3, 75.3)	48.8 (36.8, 60.7)
18 months	NE (NE, NE)	48.8 (36.8, 60.7)
Median Follow-up Time (months)	2.69	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
TEAE ≤ CTCAE Grade 2
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	76 (89.4)	167 (98.8)
Number of Subjects Censored, n (%)	9 (10.6)	2 (1.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.13)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.20, 0.66)	0.23 (0.16, 0.39)
75% percentile (95% CI)	0.72 (0.69, 1.02)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.7*	0.0, 5.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.308 (0.140)
95% CI		(0.994, 1.722)
Log-rank p-value		0.072

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
TEAE ≤ CTCAE Grade 2
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	9.6 (3.0, 16.2)	2.4 (0.1, 4.7)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.46	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
TEAE ≤ CTCAE Grade 2
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	124 (85.5)	277 (96.5)
Number of Subjects Censored, n (%)	21 (14.5)	10 (3.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.16 (0.07, 0.30)	0.10 (0.07, 0.13)
Median (95% CI)	0.59 (0.46, 0.69)	0.33 (0.26, 0.43)
75% percentile (95% CI)	0.95 (0.69, 1.64)	0.69 (NE, NE)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.532 (0.110)
95% CI		(1.234, 1.902)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
TEAE ≤ CTCAE Grade 2
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	12.6 (7.0, 18.3)	2.4 (0.4, 4.4)
6 months	NE (NE, NE)	1.6 (0.0, 3.5)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.59	0.33

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
TEAE ≥ CTCAE Grade 3
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	40 (47.1)	104 (61.5)
Number of Subjects Censored, n (%)	45 (52.9)	65 (38.5)
Time to first TEAE (months)		
25% percentile (95% CI)	1.28 (0.72, 1.87)	1.15 (0.69, 1.51)
Median (95% CI)	3.65 (2.00, NE)	3.25 (2.53, 4.70)
75% percentile (95% CI)	NE (4.83, NE)	9.20 (5.98, NE)
Min, Max	0.1, 6.8*	0.1, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.125 (0.189)
95% CI		(0.776, 1.630)
Log-rank p-value		0.458

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
TEAE ≥ CTCAE Grade 3
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	59.2 (48.6, 69.8)	52.4 (44.8, 60.1)
6 months	36.8 (20.5, 53.2)	33.1 (24.3, 41.9)
9 months	NE (NE, NE)	25.5 (16.0, 35.0)
12 months	NE (NE, NE)	10.2 (0.0, 25.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.40	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
TEAE ≥ CTCAE Grade 3
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	63 (43.4)	173 (60.3)
Number of Subjects Censored, n (%)	82 (56.6)	114 (39.7)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.69, 1.28)	0.92 (0.69, 1.15)
Median (95% CI)	5.36 (3.71, NE)	2.79 (1.87, 3.84)
75% percentile (95% CI)	9.26 (5.36, NE)	11.04 (7.62, NE)
Min, Max	0.1, 9.3	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.273 (0.151)
95% CI		(0.948, 1.710)
Log-rank p-value		0.088

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
TEAE ≥ CTCAE Grade 3
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	59.3 (51.2, 67.4)	47.2 (41.4, 53.1)
6 months	34.7 (13.5, 55.8)	38.1 (31.8, 44.5)
9 months	34.7 (13.5, 55.8)	26.8 (18.3, 35.3)
12 months	0.0 (NE, NE)	23.5 (13.8, 33.1)
18 months	0.0 (NE, NE)	15.7 (1.6, 29.7)
Median Follow-up Time (months)	2.27	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
Discontinuation due to TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	16 (18.8)	30 (17.8)
Number of Subjects Censored, n (%)	69 (81.2)	139 (82.2)
Time to first TEAE (months)		
25% percentile (95% CI)	3.98 (3.15, NE)	9.69 (5.39, NE)
Median (95% CI)	NE (4.57, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.650 (0.322)
95% CI		(0.346, 1.222)
Log-rank p-value		0.226

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
Discontinuation due to TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.2 (78.6, 93.8)	86.7 (81.4, 91.9)
6 months	57.6 (35.3, 79.9)	81.1 (74.3, 88.0)
9 months	NE (NE, NE)	76.6 (67.7, 85.5)
12 months	NE (NE, NE)	70.7 (56.9, 84.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.07

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
Discontinuation due to TEAE
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	24 (16.6)	55 (19.2)
Number of Subjects Censored, n (%)	121 (83.4)	232 (80.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	8.21 (5.26, 8.90)
Median (95% CI)	NE (NE, NE)	NE (11.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.751 (0.255)
95% CI		(0.455, 1.239)
Log-rank p-value		0.261

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
Discontinuation due to TEAE
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.7 (77.6, 89.8)	88.2 (84.5, 92.0)
6 months	78.8 (67.8, 89.8)	80.1 (74.4, 85.7)
9 months	78.8 (67.8, 89.8)	65.7 (55.7, 75.7)
12 months	78.8 (67.8, 89.8)	61.0 (48.2, 73.9)
18 months	NE (NE, NE)	61.0 (48.2, 73.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
Deaths (Grade 5 TEAEs)
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	8 (9.4)	5 (3.0)
Number of Subjects Censored, n (%)	77 (90.6)	164 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.98, NE)	NE (9.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.199 (0.623)
95% CI		(0.059, 0.674)
Log-rank p-value		0.004

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
Deaths (Grade 5 TEAEs)
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.8 (84.2, 97.3)	98.2 (96.2, 100.0)
6 months	84.3 (70.6, 98.0)	97.2 (94.4, 100.0)
9 months	NE (NE, NE)	97.2 (94.4, 100.0)
12 months	NE (NE, NE)	89.7 (75.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3H
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by RAS Status
Safety Population
Deaths (Grade 5 TEAEs)
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	8 (5.5)	14 (4.9)
Number of Subjects Censored, n (%)	137 (94.5)	273 (95.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.512 (0.472)
95% CI		(0.203, 1.292)
Log-rank p-value		0.161

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.4 (89.0, 97.9)	97.4 (95.6, 99.3)
6 months	93.4 (89.0, 97.9)	94.4 (90.9, 97.9)
9 months	93.4 (89.0, 97.9)	90.0 (84.0, 96.1)
12 months	93.4 (89.0, 97.9)	90.0 (84.0, 96.1)
18 months	NE (NE, NE)	90.0 (84.0, 96.1)
Median Follow-up Time (months)	2.83	3.75

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	180 (91.4)	392 (98.7)
Number of Subjects Censored, n (%)	17 (8.6)	5 (1.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.10 (0.07, 0.20)	0.07 (0.07, 0.10)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Median (95% CI)	0.46 (0.33, 0.59)	0.26 (0.23, 0.33)
75% percentile (95% CI)	0.69 (0.69, 0.82)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.413 (0.092)
95% CI		(1.180, 1.691)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	8.7 (4.7, 12.7)	1.7 (0.4, 3.0)
6 months	NE (NE, NE)	0.9 (0.0, 1.9)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
TEAE
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	10 (100.0)	7 (100.0)
Number of Subjects Censored, n (%)	0	0
Time to first TEAE (months)		
25% percentile (95% CI)	0.03 (0.03, 0.69)	0.26 (0.03, 0.69)
Median (95% CI)	0.67 (0.03, 0.76)	0.69 (0.03, 0.72)
75% percentile (95% CI)	0.76 (0.66, NE)	0.72 (0.62, NE)
Min, Max	0.0, 1.0	0.0, 1.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.693 (0.640)
95% CI		(0.198, 2.428)
Log-rank p-value		0.513

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
TEAE
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	0.0 (NE, NE)	0.0 (NE, NE)
6 months	0.0 (NE, NE)	0.0 (NE, NE)
9 months	0.0 (NE, NE)	0.0 (NE, NE)
12 months	0.0 (NE, NE)	0.0 (NE, NE)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.67	0.69

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
TEAE
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	21 (91.3)	51 (98.1)
Number of Subjects Censored, n (%)	2 (8.7)	1 (1.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.46)	0.07 (0.07, 0.16)
Median (95% CI)	0.53 (0.07, 0.72)	0.26 (0.16, 0.39)
75% percentile (95% CI)	1.02 (0.69, 1.87)	0.69 (0.39, 0.82)
Min, Max	0.0, 3.4*	0.0, 3.7
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.523 (0.278)
95% CI		(0.883, 2.626)
Log-rank p-value		0.157

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
TEAE
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	8.7 (0.0, 20.2)	3.8 (0.0, 9.1)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.53	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
Serious TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	65 (33.0)	135 (34.0)
Number of Subjects Censored, n (%)	132 (67.0)	262 (66.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.35 (0.95, 2.40)	2.96 (2.40, 3.61)
Median (95% CI)	NE (4.14, NE)	11.04 (7.79, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.709 (0.155)
95% CI		(0.523, 0.961)
Log-rank p-value		0.036

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
Serious TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	68.3 (61.6, 75.0)	74.5 (70.0, 78.9)
6 months	55.3 (42.7, 67.9)	62.2 (56.5, 67.9)
9 months	NE (NE, NE)	52.3 (44.1, 60.5)
12 months	NE (NE, NE)	41.3 (27.8, 54.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.63	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
Serious TEAE
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	3 (30.0)	3 (42.9)
Number of Subjects Censored, n (%)	7 (70.0)	4 (57.1)
Time to first TEAE (months)		
25% percentile (95% CI)	2.00 (0.49, NE)	0.79 (0.72, NE)
Median (95% CI)	NE (0.49, NE)	7.03 (0.72, NE)
75% percentile (95% CI)	NE (NE, NE)	7.03 (NE, NE)
Min, Max	0.5, 13.0*	0.7, 7.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.034 (0.979)
95% CI		(0.152, 7.043)
Log-rank p-value		0.692

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
Serious TEAE
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	70.0 (41.6, 98.4)	71.4 (38.0, 100.0)
6 months	70.0 (41.6, 98.4)	71.4 (38.0, 100.0)
9 months	70.0 (41.6, 98.4)	0.0 (NE, NE)
12 months	70.0 (41.6, 98.4)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.81	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
Serious TEAE
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	4 (17.4)	16 (30.8)
Number of Subjects Censored, n (%)	19 (82.6)	36 (69.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.66, NE)	2.53 (0.95, NE)
Median (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.7, 6.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.470 (0.597)
95% CI		(0.456, 4.738)
Log-rank p-value		0.462

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
Serious TEAE
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.6 (67.1, 98.1)	72.4 (60.1, 84.7)
6 months	82.6 (67.1, 98.1)	68.1 (54.0, 82.3)
9 months	NE (NE, NE)	68.1 (54.0, 82.3)
12 months	NE (NE, NE)	68.1 (54.0, 82.3)
18 months	NE (NE, NE)	68.1 (54.0, 82.3)
Median Follow-up Time (months)	2.86	3.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
TEAE ≤ CTCAE Grade 2
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	169 (85.8)	388 (97.7)
Number of Subjects Censored, n (%)	28 (14.2)	9 (2.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.10 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.53 (0.39, 0.66)	0.30 (0.23, 0.39)
75% percentile (95% CI)	0.76 (0.69, 1.35)	0.69 (NE, NE)
Min, Max	0.0, 4.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.474 (0.094)
95% CI		(1.227, 1.772)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
TEAE ≤ CTCAE Grade 2
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	12.3 (7.5, 17.2)	2.0 (0.5, 3.5)
6 months	NE (NE, NE)	1.0 (0.0, 2.2)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.53	0.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
TEAE ≤ CTCAE Grade 2
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	10 (100.0)	7 (100.0)
Number of Subjects Censored, n (%)	0	0
Time to first TEAE (months)		
25% percentile (95% CI)	0.03 (0.03, 0.69)	0.26 (0.03, 0.69)
Median (95% CI)	0.67 (0.03, 0.76)	0.69 (0.03, 0.95)
75% percentile (95% CI)	0.76 (0.66, NE)	0.95 (0.66, NE)
Min, Max	0.0, 1.0	0.0, 1.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.609 (0.654)
95% CI		(0.169, 2.196)
Log-rank p-value		0.513

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
TEAE ≤ CTCAE Grade 2
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	0.0 (NE, NE)	0.0 (NE, NE)
6 months	0.0 (NE, NE)	0.0 (NE, NE)
9 months	0.0 (NE, NE)	0.0 (NE, NE)
12 months	0.0 (NE, NE)	0.0 (NE, NE)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.67	0.69

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
TEAE ≤ CTCAE Grade 2
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	21 (91.3)	49 (94.2)
Number of Subjects Censored, n (%)	2 (8.7)	3 (5.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.46)	0.07 (0.07, 0.16)
Median (95% CI)	0.53 (0.07, 0.72)	0.26 (0.16, 0.53)
75% percentile (95% CI)	1.02 (0.69, 1.87)	0.71 (0.53, 0.85)
Min, Max	0.0, 3.4*	0.0, 3.7
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.365 (0.280)
95% CI		(0.789, 2.362)
Log-rank p-value		0.264

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
TEAE ≤ CTCAE Grade 2
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	8.7 (0.0, 20.2)	6.3 (0.0, 13.0)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.53	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
TEAE ≥ CTCAE Grade 3
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	91 (46.2)	243 (61.2)
Number of Subjects Censored, n (%)	106 (53.8)	154 (38.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.72, 1.25)	0.95 (0.69, 1.18)
Median (95% CI)	3.71 (3.15, 5.36)	2.86 (2.53, 3.65)
75% percentile (95% CI)	NE (5.36, NE)	8.90 (7.33, NE)
Min, Max	0.1, 6.8*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.144 (0.125)
95% CI		(0.896, 1.462)
Log-rank p-value		0.193

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
TEAE ≥ CTCAE Grade 3
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	58.0 (50.9, 65.0)	49.0 (44.0, 54.0)
6 months	31.3 (16.8, 45.8)	34.7 (29.1, 40.3)
9 months	NE (NE, NE)	23.6 (16.2, 31.1)
12 months	NE (NE, NE)	14.1 (3.9, 24.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.23	2.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
TEAE ≥ CTCAE Grade 3
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	5 (50.0)	5 (71.4)
Number of Subjects Censored, n (%)	5 (50.0)	2 (28.6)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.49, NE)	0.72 (0.62, 0.95)
Median (95% CI)	9.26 (0.49, NE)	0.95 (0.62, NE)
75% percentile (95% CI)	9.26 (NE, NE)	6.90 (0.79, NE)
Min, Max	0.5, 9.3	0.6, 7.0*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.193 (0.885)
95% CI		(0.210, 6.765)
Log-rank p-value		0.862

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
TEAE ≥ CTCAE Grade 3
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	60.0 (29.6, 90.4)	42.9 (6.2, 79.5)
6 months	60.0 (29.6, 90.4)	42.9 (6.2, 79.5)
9 months	60.0 (29.6, 90.4)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	0.95

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
TEAE ≥ CTCAE Grade 3
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	7 (30.4)	29 (55.8)
Number of Subjects Censored, n (%)	16 (69.6)	23 (44.2)
Time to first TEAE (months)		
25% percentile (95% CI)	1.61 (0.62, NE)	1.38 (0.62, 1.68)
Median (95% CI)	NE (1.64, NE)	3.91 (1.68, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (7.10, NE)
Min, Max	0.6, 6.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.710 (0.449)
95% CI		(0.710, 4.119)
Log-rank p-value		0.318

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
TEAE ≥ CTCAE Grade 3
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	69.6 (50.8, 88.4)	51.0 (37.2, 64.8)
6 months	69.6 (50.8, 88.4)	44.4 (29.7, 59.2)
9 months	NE (NE, NE)	40.0 (24.4, 55.6)
12 months	NE (NE, NE)	40.0 (24.4, 55.6)
18 months	NE (NE, NE)	26.7 (2.9, 50.4)
Median Follow-up Time (months)	2.83	2.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
Discontinuation due to TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	37 (18.8)	74 (18.6)
Number of Subjects Censored, n (%)	160 (81.2)	323 (81.4)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (3.15, NE)	8.21 (6.18, 11.04)
Median (95% CI)	NE (4.83, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.649 (0.210)
95% CI		(0.430, 0.980)
Log-rank p-value		0.043

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
Discontinuation due to TEAE
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.5 (78.1, 88.8)	87.3 (84.0, 90.7)
6 months	65.2 (50.9, 79.6)	80.7 (76.1, 85.3)
9 months	NE (NE, NE)	68.7 (60.4, 76.9)
12 months	NE (NE, NE)	65.0 (54.6, 75.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
Discontinuation due to TEAE
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	1 (10.0)	3 (42.9)
Number of Subjects Censored, n (%)	9 (90.0)	4 (57.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.49, NE)	4.11 (0.79, NE)
Median (95% CI)	NE (0.49, NE)	7.03 (0.79, NE)
75% percentile (95% CI)	NE (NE, NE)	7.03 (NE, NE)
Min, Max	0.5, 13.0*	0.8, 7.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.773 (1.591)
95% CI		(0.034, 17.480)
Log-rank p-value		0.808

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
Discontinuation due to TEAE
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (71.4, 100.0)	85.7 (59.8, 100.0)
6 months	90.0 (71.4, 100.0)	71.4 (38.0, 100.0)
9 months	90.0 (71.4, 100.0)	0.0 (NE, NE)
12 months	90.0 (71.4, 100.0)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.81	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
Discontinuation due to TEAE
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	2 (8.7)	8 (15.4)
Number of Subjects Censored, n (%)	21 (91.3)	44 (84.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.66, NE)	9.69 (4.17, NE)
Median (95% CI)	NE (NE, NE)	NE (9.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.226 (0.894)
95% CI		(0.212, 7.071)
Log-rank p-value		0.569

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
Discontinuation due to TEAE
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (79.8, 100.0)	90.0 (81.7, 98.3)
6 months	91.3 (79.8, 100.0)	81.9 (68.6, 95.1)
9 months	NE (NE, NE)	81.9 (68.6, 95.1)
12 months	NE (NE, NE)	73.7 (54.3, 93.0)
18 months	NE (NE, NE)	73.7 (54.3, 93.0)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
Deaths (Grade 5 TEAEs)
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	13 (6.6)	15 (3.8)
Number of Subjects Censored, n (%)	184 (93.4)	382 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.356 (0.397)
95% CI		(0.163, 0.774)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
Deaths (Grade 5 TEAEs)
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (89.0, 96.8)	97.9 (96.5, 99.3)
6 months	89.7 (82.4, 96.9)	95.3 (92.6, 98.0)
9 months	NE (NE, NE)	92.9 (88.7, 97.2)
12 months	NE (NE, NE)	92.9 (88.7, 97.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
Deaths (Grade 5 TEAEs)
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	1 (10.0)	0
Number of Subjects Censored, n (%)	9 (90.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.20, NE)	NE (NE, NE)
Median (95% CI)	NE (2.20, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.617

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
Deaths (Grade 5 TEAEs)
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (68.4, 100.0)	100.0 (100.0, 100.0)
6 months	88.9 (68.4, 100.0)	100.0 (100.0, 100.0)
9 months	88.9 (68.4, 100.0)	NE (NE, NE)
12 months	88.9 (68.4, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3I
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by BRAF Status
Safety Population
Deaths (Grade 5 TEAEs)
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	2 (8.7)	4 (7.7)
Number of Subjects Censored, n (%)	21 (91.3)	48 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.64, NE)	NE (6.18, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.542 (1.157)
95% CI		(0.056, 5.230)
Log-rank p-value		0.543

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE
<=3

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.1 (79.3, 100.0)	96.0 (90.6, 100.0)
6 months	91.1 (79.3, 100.0)	96.0 (90.6, 100.0)
9 months	NE (NE, NE)	90.7 (79.3, 100.0)
12 months	NE (NE, NE)	81.6 (61.9, 100.0)
18 months	NE (NE, NE)	81.6 (61.9, 100.0)
Median Follow-up Time (months)	2.86	3.76

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	39 (86.7)	72 (94.7)
Number of Subjects Censored, n (%)	6 (13.3)	4 (5.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.36)	0.13 (0.07, 0.23)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Median (95% CI)	0.66 (0.30, 0.69)	0.39 (0.23, 0.66)
75% percentile (95% CI)	1.28 (0.69, 3.65)	0.72 (0.66, 0.95)
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.296 (0.210)
95% CI		(0.859, 1.955)
Log-rank p-value		0.176

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	15.6 (5.0, 26.1)	6.6 (1.0, 12.2)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.66	0.39

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	172 (93.0)	378 (99.5)
Number of Subjects Censored, n (%)	13 (7.0)	2 (0.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.10 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.33, 0.56)	0.25 (0.20, 0.30)
75% percentile (95% CI)	0.69 (0.69, 0.76)	0.69 (0.62, 0.69)
Min, Max	0.0, 3.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.413 (0.094)
95% CI		(1.177, 1.697)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	6.6 (2.9, 10.2)	1.1 (0.0, 2.1)
6 months	NE (NE, NE)	0.4 (0.0, 1.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
Serious TEAE
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	11 (24.4)	21 (27.6)
Number of Subjects Censored, n (%)	34 (75.6)	55 (72.4)
Time to first TEAE (months)		
25% percentile (95% CI)	3.65 (0.89, NE)	4.90 (2.00, 8.28)
Median (95% CI)	NE (3.65, NE)	NE (7.75, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.744 (0.406)
95% CI		(0.336, 1.647)
Log-rank p-value		0.613

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
Serious TEAE
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.3 (64.8, 89.7)	79.2 (69.7, 88.6)
6 months	NE (NE, NE)	70.4 (57.6, 83.2)
9 months	NE (NE, NE)	60.3 (43.4, 77.3)
12 months	NE (NE, NE)	53.6 (34.2, 73.1)
18 months	NE (NE, NE)	53.6 (34.2, 73.1)
Median Follow-up Time (months)	2.83	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
Serious TEAE
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	61 (33.0)	133 (35.0)
Number of Subjects Censored, n (%)	124 (67.0)	247 (65.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.38 (1.02, 2.33)	2.86 (1.87, 3.48)
Median (95% CI)	NE (5.36, NE)	11.04 (7.79, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.2, 13.0*	0.1, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.760 (0.159)
95% CI		(0.557, 1.037)
Log-rank p-value		0.105

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
Serious TEAE
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	67.9 (61.0, 74.9)	73.3 (68.7, 77.8)
6 months	56.7 (44.1, 69.2)	61.9 (56.2, 67.6)
9 months	56.7 (44.1, 69.2)	53.2 (45.1, 61.2)
12 months	56.7 (44.1, 69.2)	42.9 (28.3, 57.6)
18 months	NE (NE, NE)	42.9 (28.3, 57.6)
Median Follow-up Time (months)	2.63	3.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE ≤ CTCAE Grade 2
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	36 (80.0)	71 (93.4)
Number of Subjects Censored, n (%)	9 (20.0)	5 (6.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.46)	0.13 (0.07, 0.26)
Median (95% CI)	0.66 (0.36, 0.69)	0.54 (0.26, 0.69)
75% percentile (95% CI)	1.61 (0.69, NE)	0.72 (0.69, 1.12)
Min, Max	0.0, 4.7*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.316 (0.215)
95% CI		(0.863, 2.006)
Log-rank p-value		0.240

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE ≤ CTCAE Grade 2
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	19.8 (8.0, 31.5)	7.3 (1.3, 13.3)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.66	0.54

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE ≤ CTCAE Grade 2
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	164 (88.6)	373 (98.2)
Number of Subjects Censored, n (%)	21 (11.4)	7 (1.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.10 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.49 (0.39, 0.69)	0.26 (0.23, 0.36)
75% percentile (95% CI)	0.76 (0.69, 1.02)	0.69 (NE, NE)
Min, Max	0.0, 3.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.454 (0.095)
95% CI		(1.206, 1.753)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE ≤ CTCAE Grade 2
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	9.0 (4.5, 13.5)	1.4 (0.1, 2.7)
6 months	NE (NE, NE)	0.5 (0.0, 1.3)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.49	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE ≥ CTCAE Grade 3
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	18 (40.0)	38 (50.0)
Number of Subjects Censored, n (%)	27 (60.0)	38 (50.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.62, 3.65)	1.45 (0.69, 2.00)
Median (95% CI)	4.83 (2.00, NE)	4.90 (2.63, 9.20)
75% percentile (95% CI)	NE (4.83, NE)	NE (7.10, NE)
Min, Max	0.1, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.113 (0.302)
95% CI		(0.616, 2.010)
Log-rank p-value		0.599

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE ≥ CTCAE Grade 3
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	64.2 (50.1, 78.3)	58.3 (47.0, 69.6)
6 months	NE (NE, NE)	42.8 (28.3, 57.3)
9 months	NE (NE, NE)	37.4 (21.4, 53.5)
12 months	NE (NE, NE)	30.0 (11.6, 48.3)
18 months	NE (NE, NE)	30.0 (11.6, 48.3)
Median Follow-up Time (months)	2.83	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE ≥ CTCAE Grade 3
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	85 (45.9)	239 (62.9)
Number of Subjects Censored, n (%)	100 (54.1)	141 (37.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.99 (0.72, 1.35)	0.95 (0.69, 1.15)
Median (95% CI)	4.14 (3.15, NE)	2.79 (2.00, 3.35)
75% percentile (95% CI)	9.26 (5.55, NE)	8.90 (7.33, NE)
Min, Max	0.1, 9.3	0.0, 16.1
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.221 (0.128)
95% CI		(0.950, 1.570)
Log-rank p-value		0.072

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE ≥ CTCAE Grade 3
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	57.9 (50.7, 65.2)	47.4 (42.3, 52.5)
6 months	36.3 (22.2, 50.5)	34.8 (29.3, 40.4)
9 months	36.3 (22.2, 50.5)	23.6 (16.4, 30.8)
12 months	0.0 (NE, NE)	16.8 (7.0, 26.6)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.23	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
Discontinuation due to TEAE
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	4 (8.9)	12 (15.8)
Number of Subjects Censored, n (%)	41 (91.1)	64 (84.2)
Time to first TEAE (months)		
25% percentile (95% CI)	4.83 (3.65, NE)	NE (3.52, NE)
Median (95% CI)	4.83 (3.65, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (4.83, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.252 (0.621)
95% CI		(0.370, 4.230)
Log-rank p-value		0.593

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
Discontinuation due to TEAE
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (88.1, 100.0)	88.7 (81.3, 96.1)
6 months	NE (NE, NE)	77.6 (65.2, 89.9)
9 months	NE (NE, NE)	77.6 (65.2, 89.9)
12 months	NE (NE, NE)	77.6 (65.2, 89.9)
18 months	NE (NE, NE)	77.6 (65.2, 89.9)
Median Follow-up Time (months)	2.83	3.47

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
Discontinuation due to TEAE
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	36 (19.5)	73 (19.2)
Number of Subjects Censored, n (%)	149 (80.5)	307 (80.8)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (3.15, NE)	8.21 (6.18, 9.69)
Median (95% CI)	NE (NE, NE)	NE (11.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.647 (0.212)
95% CI		(0.427, 0.981)
Log-rank p-value		0.054

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
Discontinuation due to TEAE
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.1 (76.4, 87.7)	87.4 (84.0, 90.8)
6 months	70.6 (58.8, 82.4)	81.0 (76.4, 85.7)
9 months	70.6 (58.8, 82.4)	67.7 (59.2, 76.2)
12 months	70.6 (58.8, 82.4)	61.1 (49.5, 72.8)
18 months	NE (NE, NE)	61.1 (49.5, 72.8)
Median Follow-up Time (months)	2.79	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
Deaths (Grade 5 TEAEs)
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	2 (4.4)	0
Number of Subjects Censored, n (%)	43 (95.6)	76 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.035

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
Deaths (Grade 5 TEAEs)
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (88.0, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3J
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines
Safety Population
Deaths (Grade 5 TEAEs)
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	14 (7.6)	19 (5.0)
Number of Subjects Censored, n (%)	171 (92.4)	361 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.402 (0.372)
95% CI		(0.194, 0.833)
Log-rank p-value		0.010

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE
<=3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.8 (87.4, 96.1)	97.3 (95.6, 98.9)
6 months	88.5 (80.9, 96.1)	94.6 (91.8, 97.5)
9 months	88.5 (80.9, 96.1)	91.4 (86.7, 96.1)
12 months	88.5 (80.9, 96.1)	88.0 (80.1, 95.9)
18 months	NE (NE, NE)	88.0 (80.1, 95.9)
Median Follow-up Time (months)	2.83	4.01

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	55 (85.9)	120 (96.8)
Number of Subjects Censored, n (%)	9 (14.1)	4 (3.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.21 (0.07, 0.36)	0.13 (0.07, 0.16)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Median (95% CI)	0.69 (0.46, 0.69)	0.38 (0.26, 0.46)
75% percentile (95% CI)	1.31 (0.69, 3.65)	0.69 (0.66, 0.72)
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.612 (0.169)
95% CI		(1.158, 2.244)
Log-rank p-value		0.007

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	15.6 (6.7, 24.5)	4.0 (0.6, 7.5)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.69	0.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	156 (94.0)	330 (99.4)
Number of Subjects Censored, n (%)	10 (6.0)	2 (0.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.16)	0.07 (NE, NE)
Median (95% CI)	0.46 (0.30, 0.53)	0.23 (0.16, 0.30)
75% percentile (95% CI)	0.69 (0.69, 0.72)	0.69 (0.59, 0.69)
Min, Max	0.0, 3.2*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.330 (0.099)
95% CI		(1.096, 1.613)
Log-rank p-value		0.004

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	5.5 (1.9, 9.0)	1.2 (0.0, 2.4)
6 months	NE (NE, NE)	0.4 (0.0, 1.2)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Serious TEAE
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	15 (23.4)	37 (29.8)
Number of Subjects Censored, n (%)	49 (76.6)	87 (70.2)
Time to first TEAE (months)		
25% percentile (95% CI)	3.65 (1.35, NE)	2.83 (1.87, 7.75)
Median (95% CI)	NE (3.65, NE)	NE (8.28, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.985 (0.318)
95% CI		(0.529, 1.837)
Log-rank p-value		0.863

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Serious TEAE
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.0 (66.4, 87.7)	74.9 (67.1, 82.7)
6 months	NE (NE, NE)	68.4 (59.0, 77.9)
9 months	NE (NE, NE)	62.2 (50.3, 74.1)
12 months	NE (NE, NE)	58.1 (44.5, 71.7)
18 months	NE (NE, NE)	58.1 (44.5, 71.7)
Median Follow-up Time (months)	2.83	3.33

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Serious TEAE
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	57 (34.3)	117 (35.2)
Number of Subjects Censored, n (%)	109 (65.7)	215 (64.8)
Time to first TEAE (months)		
25% percentile (95% CI)	1.28 (0.92, 2.33)	2.89 (1.87, 3.61)
Median (95% CI)	NE (4.14, NE)	11.04 (7.79, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (11.96, NE)
Min, Max	0.2, 13.0*	0.1, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.719 (0.166)
95% CI		(0.520, 0.995)
Log-rank p-value		0.063

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Serious TEAE
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	67.0 (59.7, 74.3)	74.0 (69.1, 78.9)
6 months	55.7 (43.1, 68.3)	61.4 (55.2, 67.6)
9 months	55.7 (43.1, 68.3)	51.0 (41.8, 60.1)
12 months	55.7 (43.1, 68.3)	39.3 (23.3, 55.3)
18 months	NE (NE, NE)	39.3 (23.3, 55.3)
Median Follow-up Time (months)	2.64	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE ≤ CTCAE Grade 2
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	52 (81.3)	118 (95.2)
Number of Subjects Censored, n (%)	12 (18.8)	6 (4.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.21 (0.07, 0.46)	0.13 (0.07, 0.23)
Median (95% CI)	0.69 (0.46, 0.69)	0.46 (0.33, 0.66)
75% percentile (95% CI)	1.48 (0.69, NE)	0.71 (0.69, 0.85)
Min, Max	0.0, 4.7*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.507 (0.171)
95% CI		(1.078, 2.108)
Log-rank p-value		0.034

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE ≤ CTCAE Grade 2
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	18.6 (9.0, 28.2)	4.4 (0.5, 8.2)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.69	0.46

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE ≤ CTCAE Grade 2
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	148 (89.2)	326 (98.2)
Number of Subjects Censored, n (%)	18 (10.8)	6 (1.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.16)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.33, 0.62)	0.26 (0.20, 0.33)
75% percentile (95% CI)	0.72 (0.69, 1.02)	0.69 (0.66, 0.69)
Min, Max	0.0, 3.2*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.414 (0.101)
95% CI		(1.161, 1.723)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE ≤ CTCAE Grade 2
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	8.1 (3.5, 12.7)	1.7 (0.2, 3.2)
6 months	NE (NE, NE)	0.6 (0.0, 1.6)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE ≥ CTCAE Grade 3
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	23 (35.9)	67 (54.0)
Number of Subjects Censored, n (%)	41 (64.1)	57 (46.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.54 (0.72, 3.65)	1.28 (0.69, 1.61)
Median (95% CI)	4.83 (3.65, NE)	4.70 (2.63, 7.10)
75% percentile (95% CI)	NE (4.83, NE)	NE (7.33, NE)
Min, Max	0.1, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.330 (0.249)
95% CI		(0.815, 2.168)
Log-rank p-value		0.190

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE ≥ CTCAE Grade 3
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	66.6 (54.8, 78.3)	55.8 (47.0, 64.7)
6 months	NE (NE, NE)	40.9 (30.0, 51.7)
9 months	NE (NE, NE)	30.3 (17.1, 43.4)
12 months	NE (NE, NE)	25.2 (11.0, 39.4)
18 months	NE (NE, NE)	25.2 (11.0, 39.4)
Median Follow-up Time (months)	2.81	2.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE ≥ CTCAE Grade 3
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	80 (48.2)	210 (63.3)
Number of Subjects Censored, n (%)	86 (51.8)	122 (36.7)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.69, 1.25)	0.92 (0.69, 1.15)
Median (95% CI)	3.71 (2.04, 5.55)	2.79 (1.97, 3.35)
75% percentile (95% CI)	9.26 (5.55, NE)	8.90 (6.90, NE)
Min, Max	0.1, 9.3	0.0, 16.1
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.163 (0.133)
95% CI		(0.895, 1.511)
Log-rank p-value		0.183

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE ≥ CTCAE Grade 3
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	56.3 (48.7, 64.0)	46.7 (41.3, 52.2)
6 months	35.1 (21.2, 49.0)	34.4 (28.5, 40.3)
9 months	35.1 (21.2, 49.0)	24.7 (17.3, 32.2)
12 months	0.0 (NE, NE)	17.3 (7.1, 27.6)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.12	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Discontinuation due to TEAE
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	7 (10.9)	21 (16.9)
Number of Subjects Censored, n (%)	57 (89.1)	103 (83.1)
Time to first TEAE (months)		
25% percentile (95% CI)	4.83 (3.65, NE)	8.38 (4.90, NE)
Median (95% CI)	4.83 (4.83, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (4.83, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.012 (0.460)
95% CI		(0.411, 2.493)
Log-rank p-value		0.935

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Discontinuation due to TEAE
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (83.9, 98.6)	87.3 (81.3, 93.3)
6 months	NE (NE, NE)	80.8 (72.3, 89.2)
9 months	NE (NE, NE)	73.4 (61.0, 85.8)
12 months	NE (NE, NE)	73.4 (61.0, 85.8)
18 months	NE (NE, NE)	73.4 (61.0, 85.8)
Median Follow-up Time (months)	2.83	3.56

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Discontinuation due to TEAE
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	33 (19.9)	64 (19.3)
Number of Subjects Censored, n (%)	133 (80.1)	268 (80.7)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (3.15, NE)	7.52 (5.72, 9.69)
Median (95% CI)	NE (NE, NE)	NE (11.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.644 (0.223)
95% CI		(0.416, 0.997)
Log-rank p-value		0.065

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Discontinuation due to TEAE
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.0 (76.1, 88.0)	87.8 (84.2, 91.3)
6 months	70.5 (58.5, 82.4)	80.5 (75.4, 85.5)
9 months	70.5 (58.5, 82.4)	68.6 (59.8, 77.3)
12 months	70.5 (58.5, 82.4)	61.1 (48.4, 73.8)
18 months	NE (NE, NE)	61.1 (48.4, 73.8)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Deaths (Grade 5 TEAEs)
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	5 (7.8)	0
Number of Subjects Censored, n (%)	59 (92.2)	124 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Deaths (Grade 5 TEAEs)
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.8 (83.0, 98.5)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3K
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
Deaths (Grade 5 TEAEs)
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	11 (6.6)	19 (5.7)
Number of Subjects Censored, n (%)	155 (93.4)	313 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.533 (0.397)
95% CI		(0.245, 1.161)
Log-rank p-value		0.085

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.2 (89.0, 97.3)	96.9 (94.9, 98.8)
6 months	89.8 (82.3, 97.4)	93.9 (90.6, 97.1)
9 months	89.8 (82.3, 97.4)	90.2 (84.9, 95.5)
12 months	89.8 (82.3, 97.4)	86.3 (77.2, 95.3)
18 months	NE (NE, NE)	86.3 (77.2, 95.3)
Median Follow-up Time (months)	2.83	4.07

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	202 (91.4)	435 (98.9)
Number of Subjects Censored, n (%)	19 (8.6)	5 (1.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.10 (0.07, 0.20)	0.07 (0.07, 0.10)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Median (95% CI)	0.46 (0.39, 0.59)	0.26 (0.23, 0.33)
75% percentile (95% CI)	0.72 (0.69, 0.82)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.445 (0.087)
95% CI		(1.219, 1.712)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	8.2 (4.5, 11.9)	1.6 (0.4, 2.7)
6 months	NE (NE, NE)	0.8 (0.0, 1.7)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
TEAE
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	9 (100.0)	15 (93.8)
Number of Subjects Censored, n (%)	0	1 (6.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.23 (0.03, 0.33)	0.07 (0.03, 0.07)
Median (95% CI)	0.33 (0.03, 1.35)	0.11 (0.07, 0.62)
75% percentile (95% CI)	0.69 (0.30, NE)	0.66 (0.07, NE)
Min, Max	0.0, 3.6	0.0, 3.5
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.217 (0.856)
95% CI		(0.227, 6.513)
Log-rank p-value		0.647

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
TEAE
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	11.1 (0.0, 31.6)	12.5 (0.0, 28.7)
6 months	0.0 (NE, NE)	0.0 (NE, NE)
9 months	0.0 (NE, NE)	0.0 (NE, NE)
12 months	0.0 (NE, NE)	0.0 (NE, NE)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.33	0.11

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
Serious TEAE
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	67 (30.3)	148 (33.6)
Number of Subjects Censored, n (%)	154 (69.7)	292 (66.4)
Time to first TEAE (months)		
25% percentile (95% CI)	1.58 (1.15, 3.35)	2.86 (2.17, 3.61)
Median (95% CI)	NE (5.36, NE)	11.96 (7.82, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.816 (0.151)
95% CI		(0.607, 1.097)
Log-rank p-value		0.216

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
Serious TEAE
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	70.5 (64.4, 76.7)	73.7 (69.5, 78.0)
6 months	60.7 (49.3, 72.1)	63.3 (58.0, 68.7)
9 months	60.7 (49.3, 72.1)	53.4 (45.7, 61.1)
12 months	60.7 (49.3, 72.1)	45.5 (33.3, 57.7)
18 months	NE (NE, NE)	45.5 (33.3, 57.7)
Median Follow-up Time (months)	2.79	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
Serious TEAE
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	5 (55.6)	6 (37.5)
Number of Subjects Censored, n (%)	4 (44.4)	10 (62.5)
Time to first TEAE (months)		
25% percentile (95% CI)	1.81 (0.49, NE)	4.21 (1.51, NE)
Median (95% CI)	2.30 (0.49, NE)	NE (3.61, NE)
75% percentile (95% CI)	3.65 (2.30, NE)	NE (9.23, NE)
Min, Max	0.5, 3.6	1.5, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.039 (1.600)
95% CI		(0.002, 0.887)
Log-rank p-value		0.050

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
Serious TEAE
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	44.4 (3.4, 85.5)	87.1 (70.3, 100.0)
6 months	0.0 (NE, NE)	63.3 (37.4, 89.3)
9 months	0.0 (NE, NE)	63.3 (37.4, 89.3)
12 months	0.0 (NE, NE)	50.6 (20.3, 81.0)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.57

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
TEAE ≤ CTCAE Grade 2
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	192 (86.9)	429 (97.5)
Number of Subjects Censored, n (%)	29 (13.1)	11 (2.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.10 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.56 (0.46, 0.69)	0.30 (0.26, 0.39)
75% percentile (95% CI)	0.76 (0.69, 1.25)	0.69 (NE, NE)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.477 (0.088)
95% CI		(1.242, 1.756)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
TEAE ≤ CTCAE Grade 2
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	11.4 (6.9, 15.8)	2.0 (0.6, 3.4)
6 months	NE (NE, NE)	1.0 (0.0, 2.2)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.56	0.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
TEAE ≤ CTCAE Grade 2
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	8 (88.9)	15 (93.8)
Number of Subjects Censored, n (%)	1 (11.1)	1 (6.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.23 (0.03, 0.33)	0.07 (0.03, 0.07)
Median (95% CI)	0.33 (0.03, 1.35)	0.11 (0.07, 0.69)
75% percentile (95% CI)	0.69 (0.30, NE)	0.69 (0.07, NE)
Min, Max	0.0, 4.7*	0.0, 3.5
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.710 (0.808)
95% CI		(0.146, 3.461)
Log-rank p-value		0.701

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
TEAE ≤ CTCAE Grade 2
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	11.1 (0.0, 31.6)	12.5 (0.0, 28.7)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.33	0.11

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
TEAE ≥ CTCAE Grade 3
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	98 (44.3)	266 (60.5)
Number of Subjects Censored, n (%)	123 (55.7)	174 (39.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.99 (0.72, 1.28)	0.95 (0.72, 1.22)
Median (95% CI)	4.34 (3.35, NE)	2.86 (2.53, 3.71)
75% percentile (95% CI)	9.26 (5.55, NE)	11.04 (7.39, NE)
Min, Max	0.1, 9.3	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.215 (0.120)
95% CI		(0.960, 1.537)
Log-rank p-value		0.075

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
TEAE ≥ CTCAE Grade 3
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	59.4 (52.9, 66.0)	49.1 (44.4, 53.9)
6 months	37.0 (23.3, 50.8)	36.3 (31.0, 41.6)
9 months	37.0 (23.3, 50.8)	25.4 (18.6, 32.2)
12 months	0.0 (NE, NE)	19.8 (11.0, 28.6)
18 months	0.0 (NE, NE)	13.2 (1.1, 25.2)
Median Follow-up Time (months)	2.40	2.64

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
TEAE ≥ CTCAE Grade 3
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	5 (55.6)	11 (68.8)
Number of Subjects Censored, n (%)	4 (44.4)	5 (31.3)
Time to first TEAE (months)		
25% percentile (95% CI)	1.81 (0.49, NE)	0.41 (0.07, 2.79)
Median (95% CI)	3.65 (0.49, NE)	3.20 (0.20, 9.20)
75% percentile (95% CI)	3.65 (1.87, NE)	9.20 (2.79, NE)
Min, Max	0.5, 3.6	0.1, 9.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.038 (0.858)
95% CI		(0.193, 5.576)
Log-rank p-value		0.763

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
TEAE ≥ CTCAE Grade 3
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	55.6 (23.1, 88.0)	50.0 (25.5, 74.5)
6 months	0.0 (NE, NE)	33.3 (8.4, 58.3)
9 months	0.0 (NE, NE)	33.3 (8.4, 58.3)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
Discontinuation due to TEAE
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	36 (16.3)	81 (18.4)
Number of Subjects Censored, n (%)	185 (83.7)	359 (81.6)
Time to first TEAE (months)		
25% percentile (95% CI)	4.83 (3.98, NE)	8.21 (6.18, 11.04)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.760 (0.208)
95% CI		(0.506, 1.143)
Log-rank p-value		0.209

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
Discontinuation due to TEAE
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.5 (80.7, 90.2)	87.7 (84.5, 90.8)
6 months	71.2 (58.4, 83.9)	80.6 (76.2, 85.1)
9 months	71.2 (58.4, 83.9)	70.0 (62.5, 77.5)
12 months	71.2 (58.4, 83.9)	64.6 (54.5, 74.7)
18 months	NE (NE, NE)	64.6 (54.5, 74.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
Discontinuation due to TEAE
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	4 (44.4)	4 (25.0)
Number of Subjects Censored, n (%)	5 (55.6)	12 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.79 (1.35, NE)	7.52 (1.51, NE)
Median (95% CI)	3.65 (1.35, NE)	NE (4.37, NE)
75% percentile (95% CI)	3.65 (1.81, NE)	NE (NE, NE)
Min, Max	1.2*, 3.6	1.5, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.012 (1.876)
95% CI		(0.000, 0.478)
Log-rank p-value		0.050

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
Discontinuation due to TEAE
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	62.5 (29.0, 96.0)	87.1 (70.3, 100.0)
6 months	0.0 (NE, NE)	78.3 (56.2, 100.0)
9 months	0.0 (NE, NE)	67.2 (39.4, 94.9)
12 months	0.0 (NE, NE)	67.2 (39.4, 94.9)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	5.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
Deaths (Grade 5 TEAEs)
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	15 (6.8)	18 (4.1)
Number of Subjects Censored, n (%)	206 (93.2)	422 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.363 (0.371)
95% CI		(0.176, 0.751)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
Deaths (Grade 5 TEAEs)
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.8 (89.1, 96.4)	97.6 (96.2, 99.1)
6 months	89.9 (83.4, 96.4)	95.7 (93.3, 98.1)
9 months	89.9 (83.4, 96.4)	92.8 (88.7, 96.9)
12 months	89.9 (83.4, 96.4)	90.1 (83.5, 96.7)
18 months	NE (NE, NE)	90.1 (83.5, 96.7)
Median Follow-up Time (months)	2.83	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3L
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior VEGFi
Safety Population
Deaths (Grade 5 TEAEs)
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	1 (11.1)	1 (6.3)
Number of Subjects Censored, n (%)	8 (88.9)	15 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.30, NE)	NE (3.75, NE)
Median (95% CI)	NE (2.30, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (2.30, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	1.7*, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.149 (>999)
95% CI		(0.000, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.0 (44.9, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	90.9 (73.9, 100.0)
9 months	NE (NE, NE)	90.9 (73.9, 100.0)
12 months	NE (NE, NE)	90.9 (73.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	5.04

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	83 (94.3)	177 (98.9)
Number of Subjects Censored, n (%)	5 (5.7)	2 (1.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.13)	0.07 (NE, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Median (95% CI)	0.41 (0.23, 0.53)	0.23 (0.16, 0.30)
75% percentile (95% CI)	0.69 (0.66, 0.76)	0.69 (0.59, 0.69)
Min, Max	0.0, 3.6	0.0, 5.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.238 (0.136)
95% CI		(0.950, 1.615)
Log-rank p-value		0.134

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	6.8 (1.6, 12.1)	2.2 (0.1, 4.4)
6 months	0.0 (NE, NE)	0.0 (NE, NE)
9 months	0.0 (NE, NE)	0.0 (NE, NE)
12 months	0.0 (NE, NE)	0.0 (NE, NE)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.41	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
TEAE
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	128 (90.1)	273 (98.6)
Number of Subjects Censored, n (%)	14 (9.9)	4 (1.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.16 (0.07, 0.23)	0.10 (0.07, 0.10)
Median (95% CI)	0.56 (0.39, 0.69)	0.26 (0.23, 0.39)
75% percentile (95% CI)	0.72 (0.69, 1.28)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.540 (0.110)
95% CI		(1.242, 1.909)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
TEAE
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	9.3 (4.4, 14.2)	1.7 (0.2, 3.3)
6 months	NE (NE, NE)	1.2 (0.0, 2.6)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.56	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
Serious TEAE
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	25 (28.4)	62 (34.6)
Number of Subjects Censored, n (%)	63 (71.6)	117 (65.4)
Time to first TEAE (months)		
25% percentile (95% CI)	3.15 (1.25, 4.14)	2.86 (1.77, 4.50)
Median (95% CI)	NE (3.65, NE)	11.04 (7.75, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (11.04, NE)
Min, Max	0.2, 6.8*	0.1, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.826 (0.247)
95% CI		(0.509, 1.341)
Log-rank p-value		0.605

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
Serious TEAE
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.1 (65.8, 84.4)	74.1 (67.5, 80.6)
6 months	56.2 (37.7, 74.7)	63.5 (55.3, 71.6)
9 months	NE (NE, NE)	56.6 (46.3, 67.0)
12 months	NE (NE, NE)	32.2 (9.1, 55.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
Serious TEAE
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	47 (33.1)	92 (33.2)
Number of Subjects Censored, n (%)	95 (66.9)	185 (66.8)
Time to first TEAE (months)		
25% percentile (95% CI)	1.31 (0.89, 2.30)	2.89 (2.04, 4.01)
Median (95% CI)	NE (5.36, NE)	18.04 (7.82, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.722 (0.184)
95% CI		(0.504, 1.036)
Log-rank p-value		0.091

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
Serious TEAE
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	66.5 (58.5, 74.4)	74.4 (69.1, 79.7)
6 months	59.1 (43.7, 74.5)	63.0 (56.2, 69.9)
9 months	59.1 (43.7, 74.5)	52.9 (43.2, 62.5)
12 months	59.1 (43.7, 74.5)	52.9 (43.2, 62.5)
18 months	NE (NE, NE)	52.9 (43.2, 62.5)
Median Follow-up Time (months)	2.55	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
TEAE ≤ CTCAE Grade 2
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	78 (88.6)	177 (98.9)
Number of Subjects Censored, n (%)	10 (11.4)	2 (1.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.13)	0.07 (NE, NE)
Median (95% CI)	0.46 (0.23, 0.66)	0.23 (0.16, 0.36)
75% percentile (95% CI)	0.72 (0.69, 1.25)	0.69 (0.62, 0.69)
Min, Max	0.0, 4.7*	0.0, 5.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.390 (0.138)
95% CI		(1.061, 1.821)
Log-rank p-value		0.021

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
TEAE ≤ CTCAE Grade 2
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	10.4 (3.7, 17.0)	2.2 (0.1, 4.4)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.46	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
TEAE ≤ CTCAE Grade 2
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	122 (85.9)	267 (96.4)
Number of Subjects Censored, n (%)	20 (14.1)	10 (3.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.16 (0.07, 0.26)	0.10 (0.07, 0.13)
Median (95% CI)	0.59 (0.46, 0.69)	0.36 (0.26, 0.46)
75% percentile (95% CI)	0.92 (0.69, 1.61)	0.69 (0.69, 0.72)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.472 (0.112)
95% CI		(1.183, 1.832)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
TEAE ≤ CTCAE Grade 2
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	12.2 (6.5, 17.9)	2.5 (0.4, 4.6)
6 months	NE (NE, NE)	1.7 (0.0, 3.6)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.59	0.36

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
TEAE ≥ CTCAE Grade 3
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	41 (46.6)	112 (62.6)
Number of Subjects Censored, n (%)	47 (53.4)	67 (37.4)
Time to first TEAE (months)		
25% percentile (95% CI)	1.25 (0.72, 1.87)	0.99 (0.69, 1.35)
Median (95% CI)	3.65 (2.00, NE)	3.19 (2.43, 4.57)
75% percentile (95% CI)	NE (4.83, NE)	9.20 (5.98, NE)
Min, Max	0.1, 6.8*	0.1, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.137 (0.188)
95% CI		(0.787, 1.643)
Log-rank p-value		0.428

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
TEAE ≥ CTCAE Grade 3
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	59.5 (49.2, 69.9)	51.2 (43.8, 58.6)
6 months	35.4 (18.2, 52.6)	33.2 (24.8, 41.6)
9 months	NE (NE, NE)	26.2 (17.1, 35.3)
12 months	NE (NE, NE)	8.2 (0.0, 21.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.50	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
TEAE ≥ CTCAE Grade 3
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	62 (43.7)	165 (59.6)
Number of Subjects Censored, n (%)	80 (56.3)	112 (40.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.69, 1.28)	0.92 (0.69, 1.25)
Median (95% CI)	5.36 (3.71, NE)	2.79 (1.91, 4.01)
75% percentile (95% CI)	9.26 (5.55, NE)	16.07 (7.46, NE)
Min, Max	0.1, 9.3	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.242 (0.151)
95% CI		(0.924, 1.671)
Log-rank p-value		0.100

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
TEAE ≥ CTCAE Grade 3
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	59.0 (50.8, 67.3)	47.9 (41.9, 53.9)
6 months	34.8 (13.7, 55.9)	38.4 (31.9, 44.9)
9 months	34.8 (13.7, 55.9)	26.4 (17.6, 35.2)
12 months	0.0 (NE, NE)	26.4 (17.6, 35.2)
18 months	0.0 (NE, NE)	17.6 (2.3, 32.9)
Median Follow-up Time (months)	2.27	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
Discontinuation due to TEAE
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	15 (17.0)	32 (17.9)
Number of Subjects Censored, n (%)	73 (83.0)	147 (82.1)
Time to first TEAE (months)		
25% percentile (95% CI)	3.98 (3.15, NE)	9.69 (5.39, NE)
Median (95% CI)	NE (4.57, NE)	NE (11.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.699 (0.328)
95% CI		(0.367, 1.329)
Log-rank p-value		0.373

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
Discontinuation due to TEAE
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.1 (81.1, 95.0)	87.4 (82.5, 92.3)
6 months	56.6 (32.5, 80.7)	81.4 (74.8, 88.0)
9 months	NE (NE, NE)	77.0 (68.4, 85.7)
12 months	NE (NE, NE)	64.4 (46.6, 82.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
Discontinuation due to TEAE
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	25 (17.6)	53 (19.1)
Number of Subjects Censored, n (%)	117 (82.4)	224 (80.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.94, NE)	7.46 (5.26, 8.90)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.704 (0.253)
95% CI		(0.429, 1.157)
Log-rank p-value		0.151

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
Discontinuation due to TEAE
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.5 (76.1, 88.9)	87.8 (83.9, 91.7)
6 months	77.9 (67.3, 88.5)	79.8 (74.0, 85.7)
9 months	77.9 (67.3, 88.5)	65.2 (55.0, 75.4)
12 months	77.9 (67.3, 88.5)	65.2 (55.0, 75.4)
18 months	NE (NE, NE)	65.2 (55.0, 75.4)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
Deaths (Grade 5 TEAEs)
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	7 (8.0)	5 (2.8)
Number of Subjects Censored, n (%)	81 (92.0)	174 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.98, NE)	NE (9.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.226 (0.645)
95% CI		(0.064, 0.801)
Log-rank p-value		0.014

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
Deaths (Grade 5 TEAEs)
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.6 (86.9, 98.3)	98.3 (96.4, 100.0)
6 months	85.5 (71.1, 99.9)	97.3 (94.7, 100.0)
9 months	NE (NE, NE)	97.3 (94.7, 100.0)
12 months	NE (NE, NE)	90.4 (77.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3M
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior EGFRi
Safety Population
Deaths (Grade 5 TEAEs)
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	9 (6.3)	14 (5.1)
Number of Subjects Censored, n (%)	133 (93.7)	263 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.417 (0.456)
95% CI		(0.171, 1.018)
Log-rank p-value		0.048

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE
TAS-102

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.2 (87.2, 97.2)	97.3 (95.4, 99.3)
6 months	92.2 (87.2, 97.2)	94.2 (90.6, 97.8)
9 months	92.2 (87.2, 97.2)	89.7 (83.5, 95.9)
12 months	92.2 (87.2, 97.2)	89.7 (83.5, 95.9)
18 months	NE (NE, NE)	89.7 (83.5, 95.9)
Median Follow-up Time (months)	2.83	3.78

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	108 (89.3)	233 (98.3)
Number of Subjects Censored, n (%)	13 (10.7)	4 (1.7)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.07, 0.20)	0.07 (0.07, 0.10)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Median (95% CI)	0.53 (0.39, 0.69)	0.26 (0.23, 0.39)
75% percentile (95% CI)	0.72 (0.69, 1.28)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.431 (0.119)
95% CI		(1.134, 1.805)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	10.7 (5.2, 16.2)	2.5 (0.5, 4.5)
6 months	NE (NE, NE)	0.8 (0.0, 2.3)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.53	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	18 (100.0)	39 (97.5)
Number of Subjects Censored, n (%)	0	1 (2.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.30 (0.03, 0.66)	0.13 (0.07, 0.23)
Median (95% CI)	0.67 (0.30, 0.69)	0.39 (0.23, 0.46)
75% percentile (95% CI)	0.72 (0.69, 1.38)	0.69 (0.46, 0.69)
Min, Max	0.0, 3.6	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.461 (0.303)
95% CI		(0.806, 2.649)
Log-rank p-value		0.134

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	5.6 (0.0, 16.1)	2.5 (0.0, 7.3)
6 months	0.0 (NE, NE)	NE (NE, NE)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.67	0.39

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	85 (93.4)	178 (99.4)
Number of Subjects Censored, n (%)	6 (6.6)	1 (0.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.13 (0.03, 0.23)	0.07 (0.07, 0.10)
Median (95% CI)	0.39 (0.26, 0.49)	0.23 (0.16, 0.30)
75% percentile (95% CI)	0.69 (0.59, 0.92)	0.69 (0.56, 0.69)
Min, Max	0.0, 2.8*	0.0, 3.5
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.396 (0.135)
95% CI		(1.072, 1.819)
Log-rank p-value		0.011

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	NE (NE, NE)	1.1 (0.0, 2.7)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.39	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	39 (32.2)	74 (31.2)
Number of Subjects Censored, n (%)	82 (67.8)	163 (68.8)
Time to first TEAE (months)		
25% percentile (95% CI)	1.35 (1.02, 3.35)	3.25 (2.43, 5.32)
Median (95% CI)	NE (4.14, NE)	11.04 (7.82, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.673 (0.204)
95% CI		(0.451, 1.005)
Log-rank p-value		0.064

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	69.6 (61.3, 77.9)	76.3 (70.7, 81.8)
6 months	59.9 (46.7, 73.1)	67.8 (60.8, 74.7)
9 months	59.9 (46.7, 73.1)	55.1 (44.7, 65.5)
12 months	59.9 (46.7, 73.1)	45.7 (30.2, 61.2)
18 months	NE (NE, NE)	45.7 (30.2, 61.2)
Median Follow-up Time (months)	2.83	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	5 (27.8)	13 (32.5)
Number of Subjects Censored, n (%)	13 (72.2)	27 (67.5)
Time to first TEAE (months)		
25% percentile (95% CI)	3.65 (0.66, NE)	4.07 (0.95, 5.72)
Median (95% CI)	NE (3.65, NE)	NE (4.21, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	0.2, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.789 (0.541)
95% CI		(0.273, 2.278)
Log-rank p-value		0.828

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.8 (58.6, 97.0)	76.0 (62.1, 89.9)
6 months	62.2 (30.9, 93.5)	57.7 (38.5, 76.8)
9 months	NE (NE, NE)	57.7 (38.5, 76.8)
12 months	NE (NE, NE)	57.7 (38.5, 76.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	28 (30.8)	67 (37.4)
Number of Subjects Censored, n (%)	63 (69.2)	112 (62.6)
Time to first TEAE (months)		
25% percentile (95% CI)	2.04 (0.76, NE)	2.53 (1.61, 3.61)
Median (95% CI)	NE (5.36, NE)	11.96 (6.01, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (11.96, NE)
Min, Max	0.2, 8.4*	0.1, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.864 (0.231)
95% CI		(0.549, 1.360)
Log-rank p-value		0.521

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
Serious TEAE
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	68.0 (57.9, 78.2)	71.1 (64.3, 77.9)
6 months	56.7 (34.7, 78.7)	59.0 (50.7, 67.4)
9 months	NE (NE, NE)	54.9 (45.2, 64.6)
12 months	NE (NE, NE)	41.2 (16.8, 65.6)
18 months	NE (NE, NE)	41.2 (16.8, 65.6)
Median Follow-up Time (months)	2.40	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≤ CTCAE Grade 2
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	104 (86.0)	230 (97.0)
Number of Subjects Censored, n (%)	17 (14.0)	7 (3.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.59 (0.46, 0.69)	0.33 (0.23, 0.46)
75% percentile (95% CI)	0.76 (0.69, 1.87)	0.69 (0.69, 0.72)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.464 (0.120)
95% CI		(1.157, 1.854)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≤ CTCAE Grade 2
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	13.3 (7.1, 19.5)	3.1 (0.8, 5.4)
6 months	NE (NE, NE)	1.0 (0.0, 2.8)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.59	0.33

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≤ CTCAE Grade 2
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	17 (94.4)	39 (97.5)
Number of Subjects Censored, n (%)	1 (5.6)	1 (2.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.30 (0.03, 0.66)	0.13 (0.07, 0.26)
Median (95% CI)	0.67 (0.30, 0.69)	0.39 (0.23, 0.59)
75% percentile (95% CI)	0.72 (0.69, 1.38)	0.69 (0.46, 0.72)
Min, Max	0.0, 4.7*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.340 (0.305)
95% CI		(0.737, 2.435)
Log-rank p-value		0.240

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≤ CTCAE Grade 2
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	5.6 (0.0, 16.1)	2.5 (0.0, 7.3)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.67	0.39

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≤ CTCAE Grade 2
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	79 (86.8)	175 (97.8)
Number of Subjects Censored, n (%)	12 (13.2)	4 (2.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.13 (0.03, 0.23)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.26, 0.59)	0.26 (0.20, 0.36)
75% percentile (95% CI)	0.82 (0.69, 1.61)	0.69 (0.66, 0.69)
Min, Max	0.0, 2.8*	0.0, 3.5
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.471 (0.139)
95% CI		(1.120, 1.932)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≤ CTCAE Grade 2
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	NE (NE, NE)	1.5 (0.0, 3.5)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.46	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≥ CTCAE Grade 3
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	54 (44.6)	138 (58.2)
Number of Subjects Censored, n (%)	67 (55.4)	99 (41.8)
Time to first TEAE (months)		
25% percentile (95% CI)	1.15 (0.72, 1.35)	0.99 (0.72, 1.45)
Median (95% CI)	4.14 (3.15, NE)	3.19 (2.53, 5.59)
75% percentile (95% CI)	9.26 (4.83, NE)	9.20 (7.62, NE)
Min, Max	0.1, 9.3	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.101 (0.163)
95% CI		(0.800, 1.516)
Log-rank p-value		0.452

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≥ CTCAE Grade 3
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	59.7 (50.9, 68.6)	51.6 (45.2, 58.1)
6 months	39.8 (21.8, 57.7)	40.4 (33.1, 47.7)
9 months	39.8 (21.8, 57.7)	27.5 (18.3, 36.7)
12 months	0.0 (NE, NE)	20.6 (9.7, 31.6)
18 months	0.0 (NE, NE)	20.6 (9.7, 31.6)
Median Follow-up Time (months)	2.40	2.69

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≥ CTCAE Grade 3
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	6 (33.3)	26 (65.0)
Number of Subjects Censored, n (%)	12 (66.7)	14 (35.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.66, NE)	1.00 (0.39, 1.87)
Median (95% CI)	NE (1.87, NE)	2.79 (1.64, 5.19)
75% percentile (95% CI)	NE (3.65, NE)	5.55 (4.70, NE)
Min, Max	0.7, 6.5*	0.1, 7.3
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.391 (0.461)
95% CI		(0.968, 5.908)
Log-rank p-value		0.074

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≥ CTCAE Grade 3
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.2 (51.5, 92.9)	47.8 (31.7, 63.9)
6 months	57.8 (27.5, 88.0)	19.4 (1.7, 37.0)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.83	2.45

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≥ CTCAE Grade 3
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	43 (47.3)	113 (63.1)
Number of Subjects Censored, n (%)	48 (52.7)	66 (36.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.92 (0.69, 1.81)	0.85 (0.62, 1.18)
Median (95% CI)	4.34 (2.00, 5.55)	2.60 (1.71, 3.61)
75% percentile (95% CI)	5.55 (5.36, NE)	11.96 (6.90, NE)
Min, Max	0.1, 6.4*	0.1, 16.1
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.179 (0.184)
95% CI		(0.822, 1.690)
Log-rank p-value		0.377

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE ≥ CTCAE Grade 3
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	55.9 (45.4, 66.3)	46.2 (38.7, 53.6)
6 months	22.4 (0.0, 45.8)	34.2 (26.4, 41.9)
9 months	NE (NE, NE)	30.4 (21.8, 39.0)
12 months	NE (NE, NE)	20.3 (3.1, 37.5)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.04	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
Discontinuation due to TEAE
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	17 (14.0)	48 (20.3)
Number of Subjects Censored, n (%)	104 (86.0)	189 (79.7)
Time to first TEAE (months)		
25% percentile (95% CI)	4.57 (3.98, NE)	7.52 (5.32, 11.04)
Median (95% CI)	NE (4.83, NE)	NE (11.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.941 (0.294)
95% CI		(0.529, 1.672)
Log-rank p-value		0.899

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
Discontinuation due to TEAE
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.6 (82.7, 94.5)	86.6 (82.1, 91.0)
6 months	65.2 (42.9, 87.5)	81.2 (75.5, 86.9)
9 months	65.2 (42.9, 87.5)	68.3 (58.5, 78.1)
12 months	65.2 (42.9, 87.5)	59.1 (44.1, 74.2)
18 months	NE (NE, NE)	59.1 (44.1, 74.2)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
Discontinuation due to TEAE
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	5 (27.8)	5 (12.5)
Number of Subjects Censored, n (%)	13 (72.2)	35 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	3.65 (0.66, NE)	NE (4.90, NE)
Median (95% CI)	NE (3.65, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	0.5, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.346 (0.708)
95% CI		(0.086, 1.385)
Log-rank p-value		0.129

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
Discontinuation due to TEAE
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.8 (58.6, 97.0)	92.4 (84.0, 100.0)
6 months	64.8 (36.6, 93.0)	81.2 (64.9, 97.6)
9 months	NE (NE, NE)	81.2 (64.9, 97.6)
12 months	NE (NE, NE)	81.2 (64.9, 97.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
Discontinuation due to TEAE
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	18 (19.8)	32 (17.9)
Number of Subjects Censored, n (%)	73 (80.2)	147 (82.1)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (1.54, NE)	8.21 (4.76, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.563 (0.316)
95% CI		(0.303, 1.047)
Log-rank p-value		0.067

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
Discontinuation due to TEAE
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.7 (72.4, 89.0)	88.0 (83.1, 92.8)
6 months	72.6 (55.9, 89.4)	79.6 (72.5, 86.8)
9 months	NE (NE, NE)	70.1 (58.1, 82.2)
12 months	NE (NE, NE)	70.1 (58.1, 82.2)
18 months	NE (NE, NE)	70.1 (58.1, 82.2)
Median Follow-up Time (months)	2.79	4.07

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
Deaths (Grade 5 TEAEs)
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	9 (7.4)	4 (1.7)
Number of Subjects Censored, n (%)	112 (92.6)	233 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.98, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.112 (0.655)
95% CI		(0.031, 0.403)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
Deaths (Grade 5 TEAEs)
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.6 (87.5, 97.6)	99.6 (98.8, 100.0)
6 months	87.1 (75.7, 98.5)	98.7 (96.8, 100.0)
9 months	87.1 (75.7, 98.5)	97.3 (94.0, 100.0)
12 months	87.1 (75.7, 98.5)	93.1 (84.4, 100.0)
18 months	NE (NE, NE)	93.1 (84.4, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
Deaths (Grade 5 TEAEs)
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	2 (5.0)
Number of Subjects Censored, n (%)	17 (94.4)	38 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.77, NE)	NE (6.18, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8, 6.5*	1.0*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.521 (1.330)
95% CI		(0.038, 7.056)
Log-rank p-value		0.608

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
Deaths (Grade 5 TEAEs)
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (83.9, 100.0)	97.3 (92.1, 100.0)
6 months	94.4 (83.9, 100.0)	97.3 (92.1, 100.0)
9 months	NE (NE, NE)	90.3 (76.4, 100.0)
12 months	NE (NE, NE)	90.3 (76.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3N
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior TAS-102 and/or Regorafenib
Safety Population
Deaths (Grade 5 TEAEs)
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	6 (6.6)	13 (7.3)
Number of Subjects Censored, n (%)	85 (93.4)	166 (92.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.21, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 8.4*	0.6, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.648 (0.516)
95% CI		(0.236, 1.783)
Log-rank p-value		0.389

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.8 (85.3, 98.2)	95.3 (92.2, 98.5)
6 months	91.8 (85.3, 98.2)	91.0 (85.8, 96.2)
9 months	NE (NE, NE)	86.9 (77.5, 96.2)
12 months	NE (NE, NE)	86.9 (77.5, 96.2)
18 months	NE (NE, NE)	86.9 (77.5, 96.2)
Median Follow-up Time (months)	2.79	4.37

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	143 (92.3)	330 (98.5)
Number of Subjects Censored, n (%)	12 (7.7)	5 (1.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.10 (0.07, 0.23)	0.07 (0.07, 0.10)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Median (95% CI)	0.46 (0.36, 0.59)	0.26 (0.23, 0.33)
75% percentile (95% CI)	0.69 (0.69, 0.72)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.335 (0.102)
95% CI		(1.093, 1.630)
Log-rank p-value		0.004

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	7.1 (3.0, 11.3)	2.1 (0.6, 3.6)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
TEAE
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	68 (90.7)	120 (99.2)
Number of Subjects Censored, n (%)	7 (9.3)	1 (0.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.59 (0.26, 0.69)	0.26 (0.20, 0.39)
75% percentile (95% CI)	1.02 (0.72, 1.87)	0.69 (0.59, 0.69)
Min, Max	0.0, 3.6	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.636 (0.161)
95% CI		(1.194, 2.241)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
TEAE
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	10.7 (3.7, 17.7)	1.7 (0.0, 3.9)
6 months	0.0 (NE, NE)	0.8 (0.0, 2.4)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.59	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
Serious TEAE
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	50 (32.3)	111 (33.1)
Number of Subjects Censored, n (%)	105 (67.7)	224 (66.9)
Time to first TEAE (months)		
25% percentile (95% CI)	1.28 (0.89, 2.33)	2.86 (2.00, 4.01)
Median (95% CI)	NE (NE, NE)	9.23 (7.79, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.5*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.693 (0.178)
95% CI		(0.490, 0.982)
Log-rank p-value		0.039

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
Serious TEAE
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	67.2 (59.6, 74.8)	73.9 (69.0, 78.7)
6 months	64.5 (55.6, 73.5)	62.2 (55.8, 68.7)
9 months	NE (NE, NE)	51.3 (41.4, 61.1)
12 months	NE (NE, NE)	41.4 (25.8, 57.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.40	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
Serious TEAE
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	22 (29.3)	43 (35.5)
Number of Subjects Censored, n (%)	53 (70.7)	78 (64.5)
Time to first TEAE (months)		
25% percentile (95% CI)	3.35 (1.25, 5.36)	3.19 (1.84, 4.21)
Median (95% CI)	NE (4.14, NE)	18.04 (7.79, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.836 (0.271)
95% CI		(0.492, 1.422)
Log-rank p-value		0.707

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
Serious TEAE
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.1 (65.1, 85.1)	75.3 (67.5, 83.2)
6 months	57.5 (39.3, 75.7)	65.3 (56.1, 74.5)
9 months	57.5 (39.3, 75.7)	58.8 (48.0, 69.7)
12 months	57.5 (39.3, 75.7)	51.5 (35.0, 68.0)
18 months	NE (NE, NE)	51.5 (35.0, 68.0)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
TEAE ≤ CTCAE Grade 2
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	134 (86.5)	324 (96.7)
Number of Subjects Censored, n (%)	21 (13.5)	11 (3.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.10 (0.07, 0.23)	0.07 (0.07, 0.10)
Median (95% CI)	0.53 (0.39, 0.66)	0.30 (0.23, 0.46)
75% percentile (95% CI)	0.72 (0.69, 1.02)	0.69 (NE, NE)
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.381 (0.104)
95% CI		(1.126, 1.695)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
TEAE ≤ CTCAE Grade 2
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	11.0 (5.6, 16.5)	2.7 (0.8, 4.6)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.53	0.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
TEAE ≤ CTCAE Grade 2
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	66 (88.0)	120 (99.2)
Number of Subjects Censored, n (%)	9 (12.0)	1 (0.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.59 (0.30, 0.69)	0.26 (0.23, 0.39)
75% percentile (95% CI)	1.02 (0.72, 1.87)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.643 (0.162)
95% CI		(1.196, 2.257)
Log-rank p-value		0.004

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
TEAE ≤ CTCAE Grade 2
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	12.0 (4.6, 19.4)	1.7 (0.0, 3.9)
6 months	NE (NE, NE)	0.8 (0.0, 2.4)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.59	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
TEAE ≥ CTCAE Grade 3
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	73 (47.1)	207 (61.8)
Number of Subjects Censored, n (%)	82 (52.9)	128 (38.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.76 (0.69, 1.12)	0.85 (0.69, 1.15)
Median (95% CI)	3.61 (1.87, NE)	2.79 (2.20, 3.65)
75% percentile (95% CI)	NE (NE, NE)	8.38 (6.90, NE)
Min, Max	0.1, 6.5*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.129 (0.139)
95% CI		(0.860, 1.483)
Log-rank p-value		0.384

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
TEAE ≥ CTCAE Grade 3
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	54.1 (46.1, 62.1)	48.1 (42.7, 53.5)
6 months	43.1 (29.6, 56.7)	32.7 (26.4, 38.9)
9 months	NE (NE, NE)	21.1 (12.6, 29.6)
12 months	NE (NE, NE)	12.3 (0.8, 23.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
TEAE ≥ CTCAE Grade 3
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	30 (40.0)	70 (57.9)
Number of Subjects Censored, n (%)	45 (60.0)	51 (42.1)
Time to first TEAE (months)		
25% percentile (95% CI)	1.81 (0.95, 3.65)	1.28 (0.69, 1.61)
Median (95% CI)	4.83 (3.65, NE)	3.61 (2.04, 7.33)
75% percentile (95% CI)	9.26 (5.36, NE)	16.07 (7.46, NE)
Min, Max	0.1, 9.3	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.208 (0.224)
95% CI		(0.778, 1.874)
Log-rank p-value		0.187

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
TEAE ≥ CTCAE Grade 3
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	69.8 (59.2, 80.4)	52.2 (43.2, 61.3)
6 months	35.3 (14.5, 56.0)	44.1 (34.6, 53.5)
9 months	35.3 (14.5, 56.0)	35.3 (24.4, 46.2)
12 months	0.0 (NE, NE)	29.4 (15.5, 43.3)
18 months	0.0 (NE, NE)	19.6 (1.4, 37.9)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
Discontinuation due to TEAE
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	31 (20.0)	65 (19.4)
Number of Subjects Censored, n (%)	124 (80.0)	270 (80.6)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (1.94, NE)	7.52 (5.39, 9.69)
Median (95% CI)	NE (NE, NE)	NE (11.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.603 (0.231)
95% CI		(0.383, 0.949)
Log-rank p-value		0.026

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
Discontinuation due to TEAE
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.5 (74.1, 86.9)	87.2 (83.6, 90.8)
6 months	70.5 (55.2, 85.7)	79.4 (74.0, 84.7)
9 months	NE (NE, NE)	66.7 (57.0, 76.4)
12 months	NE (NE, NE)	58.2 (44.1, 72.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
Discontinuation due to TEAE
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	9 (12.0)	20 (16.5)
Number of Subjects Censored, n (%)	66 (88.0)	101 (83.5)
Time to first TEAE (months)		
25% percentile (95% CI)	4.83 (3.98, NE)	NE (5.26, NE)
Median (95% CI)	NE (4.83, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.875 (0.424)
95% CI		(0.382, 2.008)
Log-rank p-value		0.951

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
Discontinuation due to TEAE
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.0 (87.0, 98.9)	88.9 (83.2, 94.6)
6 months	72.1 (52.8, 91.5)	83.3 (75.7, 90.9)
9 months	72.1 (52.8, 91.5)	75.7 (65.0, 86.4)
12 months	72.1 (52.8, 91.5)	75.7 (65.0, 86.4)
18 months	NE (NE, NE)	75.7 (65.0, 86.4)
Median Follow-up Time (months)	2.86	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
Deaths (Grade 5 TEAEs)
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	11 (7.1)	15 (4.5)
Number of Subjects Censored, n (%)	144 (92.9)	320 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 6.8*	0.6, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.332 (0.439)
95% CI		(0.141, 0.785)
Log-rank p-value		0.012

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
Deaths (Grade 5 TEAEs)
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.6 (86.8, 96.4)	97.5 (95.8, 99.2)
6 months	91.6 (86.8, 96.4)	95.3 (92.2, 98.3)
9 months	NE (NE, NE)	91.1 (85.4, 96.8)
12 months	NE (NE, NE)	87.1 (77.8, 96.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3O
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Liver Metastases
Safety Population
Deaths (Grade 5 TEAEs)
No

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Number of Subjects with Events, n (%)	5 (6.7)	4 (3.3)
Number of Subjects Censored, n (%)	70 (93.3)	117 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.98, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.317 (0.684)
95% CI		(0.083, 1.213)
Log-rank p-value		0.066

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=75	Fruquintinib + BSC N=121
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.0 (88.4, 99.7)	98.2 (95.8, 100.0)
6 months	89.6 (79.4, 99.7)	95.9 (92.0, 99.9)
9 months	89.6 (79.4, 99.7)	95.9 (92.0, 99.9)
12 months	89.6 (79.4, 99.7)	95.9 (92.0, 99.9)
18 months	NE (NE, NE)	95.9 (92.0, 99.9)
Median Follow-up Time (months)	2.86	4.67

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	11 (100.0)	20 (95.2)
Number of Subjects Censored, n (%)	0	1 (4.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.30)	0.07 (0.03, 0.20)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Median (95% CI)	0.30 (0.03, 0.69)	0.36 (0.07, 0.69)
75% percentile (95% CI)	0.69 (0.20, NE)	0.69 (0.46, 1.35)
Min, Max	0.0, 1.6	0.0, 3.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.750 (0.473)
95% CI		(0.297, 1.893)
Log-rank p-value		0.476

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	0.0 (NE, NE)	4.8 (0.0, 13.9)
6 months	0.0 (NE, NE)	NE (NE, NE)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.30	0.36

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	200 (91.3)	430 (98.9)
Number of Subjects Censored, n (%)	19 (8.7)	5 (1.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.10 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.39, 0.59)	0.26 (0.23, 0.30)
75% percentile (95% CI)	0.72 (0.69, 0.92)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.6*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.441 (0.087)
95% CI		(1.215, 1.710)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	8.8 (5.0, 12.6)	1.8 (0.5, 3.1)
6 months	NE (NE, NE)	0.7 (0.0, 1.7)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Serious TEAE
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	3 (27.3)	9 (42.9)
Number of Subjects Censored, n (%)	8 (72.7)	12 (57.1)
Time to first TEAE (months)		
25% percentile (95% CI)	2.40 (0.69, NE)	3.25 (0.23, 4.07)
Median (95% CI)	NE (0.69, NE)	4.21 (3.25, NE)
75% percentile (95% CI)	NE (2.40, NE)	NE (4.21, NE)
Min, Max	0.7, 6.5*	0.2, 7.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.527 (0.848)
95% CI		(0.100, 2.780)
Log-rank p-value		0.409

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Serious TEAE
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	65.5 (31.5, 99.4)	76.2 (58.0, 94.4)
6 months	65.5 (31.5, 99.4)	46.6 (21.1, 72.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Serious TEAE
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	69 (31.5)	145 (33.3)
Number of Subjects Censored, n (%)	150 (68.5)	290 (66.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.58 (1.12, 3.15)	2.89 (2.37, 4.01)
Median (95% CI)	NE (5.36, NE)	11.96 (8.28, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.751 (0.151)
95% CI		(0.559, 1.009)
Log-rank p-value		0.076

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Serious TEAE
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	69.8 (63.6, 76.0)	74.1 (69.9, 78.4)
6 months	58.1 (46.2, 69.9)	64.1 (58.8, 69.4)
9 months	58.1 (46.2, 69.9)	55.0 (47.7, 62.3)
12 months	58.1 (46.2, 69.9)	46.0 (34.3, 57.7)
18 months	NE (NE, NE)	46.0 (34.3, 57.7)
Median Follow-up Time (months)	2.79	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE ≤ CTCAE Grade 2
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	10 (90.9)	20 (95.2)
Number of Subjects Censored, n (%)	1 (9.1)	1 (4.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.30)	0.07 (0.03, 0.30)
Median (95% CI)	0.30 (0.03, 0.72)	0.46 (0.07, 0.69)
75% percentile (95% CI)	0.72 (0.20, NE)	0.69 (0.46, 1.35)
Min, Max	0.0, 1.6	0.0, 3.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.899 (0.494)
95% CI		(0.341, 2.368)
Log-rank p-value		0.503

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE ≤ CTCAE Grade 2
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	0.0 (NE, NE)	4.8 (0.0, 13.9)
6 months	0.0 (NE, NE)	NE (NE, NE)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.30	0.46

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE ≤ CTCAE Grade 2
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	190 (86.8)	424 (97.5)
Number of Subjects Censored, n (%)	29 (13.2)	11 (2.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.10 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.56 (0.46, 0.69)	0.30 (0.23, 0.39)
75% percentile (95% CI)	0.76 (0.69, 1.25)	0.69 (NE, NE)
Min, Max	0.0, 4.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.465 (0.089)
95% CI		(1.231, 1.743)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE ≤ CTCAE Grade 2
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	11.7 (7.2, 16.1)	2.3 (0.8, 3.8)
6 months	NE (NE, NE)	0.9 (0.0, 2.1)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.56	0.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE ≥ CTCAE Grade 3
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	5 (45.5)	12 (57.1)
Number of Subjects Censored, n (%)	6 (54.5)	9 (42.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.72 (0.69, NE)	1.28 (0.20, 1.61)
Median (95% CI)	NE (0.69, NE)	3.25 (1.28, NE)
75% percentile (95% CI)	NE (2.00, NE)	NE (3.25, NE)
Min, Max	0.7, 6.5*	0.2, 7.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.483 (0.680)
95% CI		(0.127, 1.834)
Log-rank p-value		0.225

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI -H/dMMR
Safety Population
TEAE ≥ CTCAE Grade 3
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	50.9 (19.1, 82.8)	52.4 (31.0, 73.7)
6 months	50.9 (19.1, 82.8)	38.8 (15.9, 61.7)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE ≥ CTCAE Grade 3
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	98 (44.7)	265 (60.9)
Number of Subjects Censored, n (%)	121 (55.3)	170 (39.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.99 (0.76, 1.28)	0.95 (0.69, 1.18)
Median (95% CI)	4.14 (3.35, 5.55)	2.86 (2.53, 3.71)
75% percentile (95% CI)	9.26 (5.55, NE)	9.20 (7.39, NE)
Min, Max	0.1, 9.3	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.201 (0.120)
95% CI		(0.949, 1.521)
Log-rank p-value		0.083

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
TEAE ≥ CTCAE Grade 3
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	59.5 (52.9, 66.1)	49.0 (44.2, 53.8)
6 months	34.8 (20.7, 48.9)	36.1 (30.8, 41.4)
9 months	34.8 (20.7, 48.9)	25.9 (19.4, 32.5)
12 months	0.0 (NE, NE)	19.0 (10.4, 27.6)
18 months	0.0 (NE, NE)	12.7 (1.0, 24.3)
Median Follow-up Time (months)	2.40	2.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Discontinuation due to TEAE
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Number of Subjects with Events, n (%)	3 (27.3)	4 (19.0)
Number of Subjects Censored, n (%)	8 (72.7)	17 (81.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.66, NE)	8.21 (0.59, NE)
Median (95% CI)	NE (0.69, NE)	8.21 (8.21, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (8.21, NE)
Min, Max	0.7, 6.5*	0.6, 8.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.076 (1.083)
95% CI		(0.009, 0.635)
Log-rank p-value		0.008

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Discontinuation due to TEAE
Yes

Statistics	Placebo + BSC N=11	Fruquintinib + BSC N=21
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.7 (46.4, 99.0)	90.2 (77.3, 100.0)
6 months	72.7 (46.4, 99.0)	82.0 (62.7, 100.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.37

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Discontinuation due to TEAE
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	37 (16.9)	81 (18.6)
Number of Subjects Censored, n (%)	182 (83.1)	354 (81.4)
Time to first TEAE (months)		
25% percentile (95% CI)	4.57 (3.65, NE)	8.21 (6.18, 11.04)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.729 (0.207)
95% CI		(0.486, 1.094)
Log-rank p-value		0.146

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Discontinuation due to TEAE
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.2 (80.4, 90.0)	87.5 (84.3, 90.7)
6 months	68.8 (55.6, 82.0)	80.4 (76.0, 84.9)
9 months	68.8 (55.6, 82.0)	70.6 (63.4, 77.7)
12 months	68.8 (55.6, 82.0)	65.6 (56.1, 75.1)
18 months	NE (NE, NE)	65.6 (56.1, 75.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Deaths (Grade 5 TEAEs)
Yes

Statistics
No events in both arms for this subgroup. No statistics were calculated.

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3P
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Prior Treatment with Immune Checkpoint Inhibitors for MSI-H/dMMR
Safety Population
Deaths (Grade 5 TEAEs)
No

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Number of Subjects with Events, n (%)	16 (7.3)	19 (4.4)
Number of Subjects Censored, n (%)	203 (92.7)	416 (95.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.358 (0.360)
95% CI		(0.177, 0.726)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE
Single

Statistics	Placebo + BSC N=219	Fruquintinib + BSC N=435
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.1 (88.2, 96.0)	97.6 (96.1, 99.1)
6 months	89.3 (82.7, 95.9)	95.2 (92.7, 97.8)
9 months	89.3 (82.7, 95.9)	92.5 (88.4, 96.5)
12 months	89.3 (82.7, 95.9)	90.1 (83.9, 96.2)
18 months	NE (NE, NE)	90.1 (83.9, 96.2)
Median Follow-up Time (months)	2.83	3.94

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	40 (88.9)	58 (96.7)
Number of Subjects Censored, n (%)	5 (11.1)	2 (3.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.23)	0.13 (0.07, 0.26)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Median (95% CI)	0.53 (0.23, 0.69)	0.38 (0.26, 0.56)
75% percentile (95% CI)	0.69 (0.69, 1.94)	0.69 (0.56, 0.69)
Min, Max	0.0, 3.6	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.379 (0.228)
95% CI		(0.881, 2.157)
Log-rank p-value		0.129

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	13.3 (3.4, 23.3)	5.0 (0.0, 10.5)
6 months	0.0 (NE, NE)	2.5 (0.0, 6.9)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.53	0.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	170 (92.4)	392 (99.0)
Number of Subjects Censored, n (%)	14 (7.6)	4 (1.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.11 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.39, 0.59)	0.23 (0.20, 0.30)
75% percentile (95% CI)	0.71 (0.69, 0.82)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.416 (0.093)
95% CI		(1.179, 1.700)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	7.1 (3.3, 10.9)	1.5 (0.3, 2.7)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Serious TEAE
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	11 (24.4)	12 (20.0)
Number of Subjects Censored, n (%)	34 (75.6)	48 (80.0)
Time to first TEAE (months)		
25% percentile (95% CI)	3.65 (1.15, NE)	NE (2.76, NE)
Median (95% CI)	NE (3.65, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.649 (0.474)
95% CI		(0.256, 1.644)
Log-rank p-value		0.429

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Serious TEAE
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.3 (64.9, 89.7)	84.8 (75.7, 94.0)
6 months	69.6 (51.4, 87.8)	77.9 (66.6, 89.2)
9 months	69.6 (51.4, 87.8)	77.9 (66.6, 89.2)
12 months	69.6 (51.4, 87.8)	77.9 (66.6, 89.2)
18 months	NE (NE, NE)	77.9 (66.6, 89.2)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Serious TEAE
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	60 (32.6)	142 (35.9)
Number of Subjects Censored, n (%)	124 (67.4)	254 (64.1)
Time to first TEAE (months)		
25% percentile (95% CI)	1.38 (0.95, 2.33)	2.83 (1.97, 3.25)
Median (95% CI)	NE (5.36, NE)	9.23 (7.79, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.1, 8.4*	0.1, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.777 (0.159)
95% CI		(0.569, 1.061)
Log-rank p-value		0.128

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Serious TEAE
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	67.7 (60.7, 74.7)	72.6 (68.1, 77.1)
6 months	57.3 (44.0, 70.5)	60.9 (55.2, 66.7)
9 months	NE (NE, NE)	50.5 (42.5, 58.5)
12 months	NE (NE, NE)	39.8 (26.7, 53.0)
18 months	NE (NE, NE)	39.8 (26.7, 53.0)
Median Follow-up Time (months)	2.58	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE ≤ CTCAE Grade 2
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	39 (86.7)	58 (96.7)
Number of Subjects Censored, n (%)	6 (13.3)	2 (3.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.23)	0.15 (0.07, 0.26)
Median (95% CI)	0.53 (0.23, 0.69)	0.39 (0.26, 0.62)
75% percentile (95% CI)	0.76 (0.69, 1.94)	0.69 (0.62, 0.72)
Min, Max	0.0, 4.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.379 (0.230)
95% CI		(0.879, 2.164)
Log-rank p-value		0.233

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE ≤ CTCAE Grade 2
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	13.3 (3.4, 23.3)	5.0 (0.0, 10.5)
6 months	NE (NE, NE)	2.5 (0.0, 6.9)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.53	0.39

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE ≤ CTCAE Grade 2
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	160 (87.0)	386 (97.5)
Number of Subjects Censored, n (%)	24 (13.0)	10 (2.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.11 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.54 (0.46, 0.69)	0.26 (0.23, 0.39)
75% percentile (95% CI)	0.76 (0.69, 1.25)	0.69 (NE, NE)
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.454 (0.096)
95% CI		(1.205, 1.753)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE ≤ CTCAE Grade 2
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	10.8 (6.0, 15.7)	1.9 (0.4, 3.4)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.54	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE ≥ CTCAE Grade 3
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	15 (33.3)	28 (46.7)
Number of Subjects Censored, n (%)	30 (66.7)	32 (53.3)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.69, 4.83)	1.20 (0.69, 2.63)
Median (95% CI)	4.83 (3.65, NE)	5.98 (2.63, NE)
75% percentile (95% CI)	9.26 (4.83, NE)	NE (NE, NE)
Min, Max	0.2, 9.3	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.357 (0.361)
95% CI		(0.669, 2.754)
Log-rank p-value		0.323

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE ≥ CTCAE Grade 3
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.1 (60.1, 86.2)	61.1 (48.5, 73.6)
6 months	42.7 (6.0, 79.4)	47.1 (32.4, 61.9)
9 months	42.7 (6.0, 79.4)	47.1 (32.4, 61.9)
12 months	0.0 (NE, NE)	47.1 (32.4, 61.9)
18 months	0.0 (NE, NE)	47.1 (32.4, 61.9)
Median Follow-up Time (months)	2.83	2.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE ≥ CTCAE Grade 3
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	87 (47.3)	249 (62.9)
Number of Subjects Censored, n (%)	97 (52.7)	147 (37.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.72, 1.25)	0.94 (0.69, 1.18)
Median (95% CI)	3.71 (2.00, 5.55)	2.79 (2.04, 3.52)
75% percentile (95% CI)	NE (5.55, NE)	8.38 (7.10, 11.96)
Min, Max	0.1, 6.8*	0.0, 16.1
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.163 (0.127)
95% CI		(0.907, 1.491)
Log-rank p-value		0.166

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
TEAE ≥ CTCAE Grade 3
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	55.5 (48.2, 62.8)	47.4 (42.4, 52.4)
6 months	34.2 (19.5, 48.9)	34.5 (29.0, 40.0)
9 months	NE (NE, NE)	22.4 (15.3, 29.4)
12 months	NE (NE, NE)	14.4 (5.5, 23.4)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.02	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Discontinuation due to TEAE
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	5 (11.1)	10 (16.7)
Number of Subjects Censored, n (%)	40 (88.9)	50 (83.3)
Time to first TEAE (months)		
25% percentile (95% CI)	4.83 (3.65, NE)	NE (2.76, NE)
Median (95% CI)	NE (4.83, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (4.83, NE)	NE (NE, NE)
Min, Max	0.7, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.858 (0.697)
95% CI		(0.474, 7.288)
Log-rank p-value		0.435

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Discontinuation due to TEAE
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.3 (86.0, 100.0)	86.4 (77.6, 95.2)
6 months	56.0 (9.5, 100.0)	81.8 (71.5, 92.2)
9 months	56.0 (9.5, 100.0)	81.8 (71.5, 92.2)
12 months	56.0 (9.5, 100.0)	81.8 (71.5, 92.2)
18 months	NE (NE, NE)	81.8 (71.5, 92.2)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Discontinuation due to TEAE
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	35 (19.0)	75 (18.9)
Number of Subjects Censored, n (%)	149 (81.0)	321 (81.1)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (3.15, NE)	7.52 (5.72, 9.69)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.627 (0.215)
95% CI		(0.412, 0.956)
Log-rank p-value		0.030

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Discontinuation due to TEAE
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.3 (76.6, 88.0)	87.9 (84.6, 91.1)
6 months	69.4 (56.4, 82.4)	80.3 (75.5, 85.1)
9 months	NE (NE, NE)	67.7 (59.5, 75.9)
12 months	NE (NE, NE)	62.0 (51.2, 72.8)
18 months	NE (NE, NE)	62.0 (51.2, 72.8)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Deaths (Grade 5 TEAEs)
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.2)	1 (1.7)
Number of Subjects Censored, n (%)	44 (97.8)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.947 (>999)
95% CI		(0.000, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Deaths (Grade 5 TEAEs)
Single

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (91.9, 100.0)	100.0 (100.0, 100.0)
6 months	97.2 (91.9, 100.0)	97.6 (92.8, 100.0)
9 months	97.2 (91.9, 100.0)	97.6 (92.8, 100.0)
12 months	97.2 (91.9, 100.0)	97.6 (92.8, 100.0)
18 months	NE (NE, NE)	97.6 (92.8, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3Q
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites Other than Colon or Rectum
Safety Population
Deaths (Grade 5 TEAEs)
Multiple

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	15 (8.2)	18 (4.5)
Number of Subjects Censored, n (%)	169 (91.8)	378 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.339 (0.371)
95% CI		(0.164, 0.702)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
TEAE
Single

Statistics	Placebo + BSC N=184	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.1 (86.6, 95.6)	97.4 (95.7, 99.0)
6 months	87.5 (79.2, 95.7)	95.2 (92.5, 97.9)
9 months	NE (NE, NE)	92.0 (87.6, 96.5)
12 months	NE (NE, NE)	89.2 (82.1, 96.2)
18 months	NE (NE, NE)	89.2 (82.1, 96.2)
Median Follow-up Time (months)	2.83	3.75

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	37 (88.1)	58 (96.7)
Number of Subjects Censored, n (%)	5 (11.9)	2 (3.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.23)	0.13 (0.07, 0.26)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
TEAE
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Median (95% CI)	0.59 (0.23, 0.69)	0.38 (0.26, 0.56)
75% percentile (95% CI)	0.92 (0.69, NE)	0.69 (0.56, 0.69)
Min, Max	0.0, 3.6	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.505 (0.238)
95% CI		(0.944, 2.398)
Log-rank p-value		0.071

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
TEAE
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	14.3 (3.7, 24.9)	5.0 (0.0, 10.5)
6 months	0.0 (NE, NE)	2.5 (0.0, 6.9)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.59	0.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
TEAE
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	174 (92.6)	392 (99.0)
Number of Subjects Censored, n (%)	14 (7.4)	4 (1.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.11 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.39, 0.59)	0.23 (0.20, 0.30)
75% percentile (95% CI)	0.69 (0.69, 0.82)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.399 (0.093)
95% CI		(1.167, 1.677)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
TEAE
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	6.9 (3.2, 10.7)	1.5 (0.3, 2.7)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
Serious TEAE
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	11 (26.2)	12 (20.0)
Number of Subjects Censored, n (%)	31 (73.8)	48 (80.0)
Time to first TEAE (months)		
25% percentile (95% CI)	3.35 (1.15, NE)	NE (2.76, NE)
Median (95% CI)	NE (3.35, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.572 (0.477)
95% CI		(0.225, 1.456)
Log-rank p-value		0.294

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
Serious TEAE
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.0 (65.3, 90.8)	84.8 (75.7, 94.0)
6 months	62.4 (40.6, 84.3)	77.9 (66.6, 89.2)
9 months	62.4 (40.6, 84.3)	77.9 (66.6, 89.2)
12 months	62.4 (40.6, 84.3)	77.9 (66.6, 89.2)
18 months	NE (NE, NE)	77.9 (66.6, 89.2)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
Serious TEAE
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	61 (32.4)	142 (35.9)
Number of Subjects Censored, n (%)	127 (67.6)	254 (64.1)
Time to first TEAE (months)		
25% percentile (95% CI)	1.38 (0.95, 2.33)	2.83 (1.97, 3.25)
Median (95% CI)	NE (5.36, NE)	9.23 (7.79, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.1, 8.4*	0.1, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.783 (0.158)
95% CI		(0.575, 1.068)
Log-rank p-value		0.138

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
Serious TEAE
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	67.9 (61.0, 74.8)	72.6 (68.1, 77.1)
6 months	57.7 (44.5, 70.8)	60.9 (55.2, 66.7)
9 months	NE (NE, NE)	50.5 (42.5, 58.5)
12 months	NE (NE, NE)	39.8 (26.7, 53.0)
18 months	NE (NE, NE)	39.8 (26.7, 53.0)
Median Follow-up Time (months)	2.61	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
TEAE ≤ CTCAE Grade 2
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	36 (85.7)	58 (96.7)
Number of Subjects Censored, n (%)	6 (14.3)	2 (3.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.23)	0.15 (0.07, 0.26)
Median (95% CI)	0.59 (0.23, 0.69)	0.39 (0.26, 0.62)
75% percentile (95% CI)	0.92 (0.69, NE)	0.69 (0.62, 0.72)
Min, Max	0.0, 4.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.466 (0.238)
95% CI		(0.920, 2.335)
Log-rank p-value		0.158

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
TEAE ≤ CTCAE Grade 2
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	14.3 (3.7, 24.9)	5.0 (0.0, 10.5)
6 months	NE (NE, NE)	2.5 (0.0, 6.9)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.59	0.39

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
TEAE ≤ CTCAE Grade 2
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	164 (87.2)	386 (97.5)
Number of Subjects Censored, n (%)	24 (12.8)	10 (2.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.11 (0.07, 0.20)	0.07 (0.07, 0.10)
Median (95% CI)	0.54 (0.46, 0.66)	0.26 (0.23, 0.39)
75% percentile (95% CI)	0.76 (0.69, 1.15)	0.69 (NE, NE)
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.441 (0.095)
95% CI		(1.197, 1.734)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
TEAE ≤ CTCAE Grade 2
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	10.6 (5.9, 15.4)	1.9 (0.4, 3.4)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.54	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
TEAE ≥ CTCAE Grade 3
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	15 (35.7)	28 (46.7)
Number of Subjects Censored, n (%)	27 (64.3)	32 (53.3)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.69, 4.83)	1.20 (0.69, 2.63)
Median (95% CI)	4.83 (3.35, NE)	5.98 (2.63, NE)
75% percentile (95% CI)	9.26 (4.83, NE)	NE (NE, NE)
Min, Max	0.2, 9.3	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.229 (0.362)
95% CI		(0.604, 2.499)
Log-rank p-value		0.515

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
TEAE ≥ CTCAE Grade 3
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.6 (60.2, 87.0)	61.1 (48.5, 73.6)
6 months	36.8 (3.2, 70.4)	47.1 (32.4, 61.9)
9 months	36.8 (3.2, 70.4)	47.1 (32.4, 61.9)
12 months	0.0 (NE, NE)	47.1 (32.4, 61.9)
18 months	0.0 (NE, NE)	47.1 (32.4, 61.9)
Median Follow-up Time (months)	2.83	2.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
TEAE ≥ CTCAE Grade 3
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	88 (46.8)	249 (62.9)
Number of Subjects Censored, n (%)	100 (53.2)	147 (37.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.72, 1.25)	0.94 (0.69, 1.18)
Median (95% CI)	4.14 (2.04, 5.55)	2.79 (2.04, 3.52)
75% percentile (95% CI)	NE (5.55, NE)	8.38 (7.10, 11.96)
Min, Max	0.1, 6.8*	0.0, 16.1
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.178 (0.126)
95% CI		(0.920, 1.508)
Log-rank p-value		0.136

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
TEAE ≥ CTCAE Grade 3
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	56.0 (48.7, 63.2)	47.4 (42.4, 52.4)
6 months	34.8 (20.0, 49.6)	34.5 (29.0, 40.0)
9 months	NE (NE, NE)	22.4 (15.3, 29.4)
12 months	NE (NE, NE)	14.4 (5.5, 23.4)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.12	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
Discontinuation due to TEAE
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	5 (11.9)	10 (16.7)
Number of Subjects Censored, n (%)	37 (88.1)	50 (83.3)
Time to first TEAE (months)		
25% percentile (95% CI)	4.83 (3.65, NE)	NE (2.76, NE)
Median (95% CI)	NE (4.83, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (4.83, NE)	NE (NE, NE)
Min, Max	0.7, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.742 (0.698)
95% CI		(0.444, 6.839)
Log-rank p-value		0.444

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
Discontinuation due to TEAE
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (85.1, 100.0)	86.4 (77.6, 95.2)
6 months	62.7 (24.6, 100.0)	81.8 (71.5, 92.2)
9 months	62.7 (24.6, 100.0)	81.8 (71.5, 92.2)
12 months	62.7 (24.6, 100.0)	81.8 (71.5, 92.2)
18 months	NE (NE, NE)	81.8 (71.5, 92.2)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
Discontinuation due to TEAE
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	35 (18.6)	75 (18.9)
Number of Subjects Censored, n (%)	153 (81.4)	321 (81.1)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (3.15, NE)	7.52 (5.72, 9.69)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.645 (0.215)
95% CI		(0.423, 0.983)
Log-rank p-value		0.042

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
Discontinuation due to TEAE
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.7 (77.1, 88.3)	87.9 (84.6, 91.1)
6 months	69.9 (57.0, 82.8)	80.3 (75.5, 85.1)
9 months	NE (NE, NE)	67.7 (59.5, 75.9)
12 months	NE (NE, NE)	62.0 (51.2, 72.8)
18 months	NE (NE, NE)	62.0 (51.2, 72.8)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
Deaths (Grade 5 TEAEs)
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Number of Subjects with Events, n (%)	1 (2.4)	1 (1.7)
Number of Subjects Censored, n (%)	41 (97.6)	59 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 13.0*	1.5*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.977 (>999)
95% CI		(0.000, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
Deaths (Grade 5 TEAEs)
Single

Statistics	Placebo + BSC N=42	Fruquintinib + BSC N=60
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.0 (91.1, 100.0)	100.0 (100.0, 100.0)
6 months	97.0 (91.1, 100.0)	97.6 (92.8, 100.0)
9 months	97.0 (91.1, 100.0)	97.6 (92.8, 100.0)
12 months	97.0 (91.1, 100.0)	97.6 (92.8, 100.0)
18 months	NE (NE, NE)	97.6 (92.8, 100.0)
Median Follow-up Time (months)	2.83	4.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3R
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Number of Metastatic Tumor Sites
Safety Population
Deaths (Grade 5 TEAEs)
Multiple

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Number of Subjects with Events, n (%)	15 (8.0)	18 (4.5)
Number of Subjects Censored, n (%)	173 (92.0)	378 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.347 (0.371)
95% CI		(0.168, 0.720)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
TEAE
< 18.5

Statistics	Placebo + BSC N=188	Fruquintinib + BSC N=396
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (87.0, 95.7)	97.4 (95.7, 99.0)
6 months	87.8 (79.9, 95.8)	95.2 (92.5, 97.9)
9 months	NE (NE, NE)	92.0 (87.6, 96.5)
12 months	NE (NE, NE)	89.2 (82.1, 96.2)
18 months	NE (NE, NE)	89.2 (82.1, 96.2)
Median Follow-up Time (months)	2.83	3.75

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	14 (100.0)	20 (100.0)
Number of Subjects Censored, n (%)	0	0
Time to first TEAE (months)		
25% percentile (95% CI)	0.16 (0.03, 0.39)	0.11 (0.03, 0.26)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
TEAE
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Median (95% CI)	0.39 (0.03, 0.69)	0.33 (0.10, 0.69)
75% percentile (95% CI)	0.69 (0.39, NE)	0.69 (0.36, 0.82)
Min, Max	0.0, 1.6	0.0, 1.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.270 (0.401)
95% CI		(0.579, 2.788)
Log-rank p-value		0.720

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
TEAE
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	0.0 (NE, NE)	0.0 (NE, NE)
6 months	0.0 (NE, NE)	0.0 (NE, NE)
9 months	0.0 (NE, NE)	0.0 (NE, NE)
12 months	0.0 (NE, NE)	0.0 (NE, NE)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.39	0.33

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
TEAE
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	69 (90.8)	138 (98.6)
Number of Subjects Censored, n (%)	7 (9.2)	2 (1.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.20 (0.07, 0.30)	0.10 (0.07, 0.10)
Median (95% CI)	0.53 (0.36, 0.69)	0.23 (0.16, 0.36)
75% percentile (95% CI)	0.72 (0.69, 1.35)	0.67 (0.46, 0.69)
Min, Max	0.0, 3.6	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.619 (0.154)
95% CI		(1.197, 2.190)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
TEAE
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	10.4 (3.5, 17.3)	1.4 (0.0, 3.4)
6 months	0.0 (NE, NE)	1.4 (0.0, 3.4)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.53	0.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
TEAE
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	123 (91.1)	281 (98.6)
Number of Subjects Censored, n (%)	12 (8.9)	4 (1.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.13)	0.07 (0.07, 0.10)
Median (95% CI)	0.46 (0.30, 0.62)	0.26 (0.23, 0.36)
75% percentile (95% CI)	0.69 (0.69, 0.95)	0.69 (0.66, 0.69)
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.316 (0.111)
95% CI		(1.058, 1.636)
Log-rank p-value		0.020

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
TEAE
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	8.3 (3.6, 13.1)	2.4 (0.6, 4.2)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.46	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
Serious TEAE
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	1 (7.1)	13 (65.0)
Number of Subjects Censored, n (%)	13 (92.9)	7 (35.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.39, NE)	1.40 (0.16, 1.84)
Median (95% CI)	NE (NE, NE)	2.69 (1.35, 8.28)
75% percentile (95% CI)	NE (NE, NE)	8.28 (2.86, NE)
Min, Max	0.4, 4.1*	0.2, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		11.958 (1.114)
95% CI		(1.346, 106.240)
Log-rank p-value		0.024

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
Serious TEAE
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (79.4, 100.0)	43.3 (20.9, 65.8)
6 months	NE (NE, NE)	36.1 (13.4, 58.8)
9 months	NE (NE, NE)	24.1 (0.0, 48.6)
12 months	NE (NE, NE)	24.1 (0.0, 48.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
Serious TEAE
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	24 (31.6)	56 (40.0)
Number of Subjects Censored, n (%)	52 (68.4)	84 (60.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.31 (0.79, NE)	2.17 (1.61, 2.89)
Median (95% CI)	NE (NE, NE)	7.79 (4.90, 11.96)
75% percentile (95% CI)	NE (NE, NE)	NE (9.23, NE)
Min, Max	0.2, 8.4*	0.1, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.039 (0.255)
95% CI		(0.630, 1.712)
Log-rank p-value		0.839

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
Serious TEAE
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	68.8 (58.1, 79.4)	66.8 (58.7, 74.9)
6 months	64.5 (51.6, 77.4)	58.2 (48.9, 67.5)
9 months	NE (NE, NE)	43.8 (27.9, 59.7)
12 months	NE (NE, NE)	25.0 (1.8, 48.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.53	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
Serious TEAE
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	45 (33.3)	83 (29.1)
Number of Subjects Censored, n (%)	90 (66.7)	202 (70.9)
Time to first TEAE (months)		
25% percentile (95% CI)	1.58 (0.95, 3.15)	4.07 (2.96, 5.32)
Median (95% CI)	5.36 (4.14, NE)	18.04 (11.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.559 (0.194)
95% CI		(0.382, 0.819)
Log-rank p-value		0.007

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
Serious TEAE
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	68.8 (60.8, 76.8)	79.7 (74.9, 84.5)
6 months	49.4 (28.8, 70.0)	67.0 (60.4, 73.6)
9 months	49.4 (28.8, 70.0)	60.5 (52.3, 68.6)
12 months	49.4 (28.8, 70.0)	54.4 (41.0, 67.8)
18 months	NE (NE, NE)	54.4 (41.0, 67.8)
Median Follow-up Time (months)	2.79	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
TEAE ≤ CTCAE Grade 2
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	14 (100.0)	20 (100.0)
Number of Subjects Censored, n (%)	0	0
Time to first TEAE (months)		
25% percentile (95% CI)	0.16 (0.03, 0.39)	0.18 (0.03, 0.30)
Median (95% CI)	0.43 (0.03, 0.69)	0.41 (0.13, 0.69)
75% percentile (95% CI)	0.69 (0.39, NE)	0.69 (0.46, 0.82)
Min, Max	0.0, 1.6	0.0, 1.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.197 (0.405)
95% CI		(0.541, 2.649)
Log-rank p-value		0.602

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
TEAE ≤ CTCAE Grade 2
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	0.0 (NE, NE)	0.0 (NE, NE)
6 months	0.0 (NE, NE)	0.0 (NE, NE)
9 months	0.0 (NE, NE)	0.0 (NE, NE)
12 months	0.0 (NE, NE)	0.0 (NE, NE)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	0.43	0.41

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
TEAE ≤ CTCAE Grade 2
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	63 (82.9)	137 (97.9)
Number of Subjects Censored, n (%)	13 (17.1)	3 (2.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.20 (0.07, 0.30)	0.10 (0.07, 0.13)
Median (95% CI)	0.62 (0.39, 0.69)	0.26 (0.20, 0.43)
75% percentile (95% CI)	0.92 (0.69, 2.76)	0.69 (0.59, 0.69)
Min, Max	0.0, 4.7*	0.0, 6.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.737 (0.158)
95% CI		(1.274, 2.369)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
TEAE ≤ CTCAE Grade 2
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	14.3 (5.8, 22.8)	1.5 (0.0, 3.6)
6 months	NE (NE, NE)	1.5 (0.0, 3.6)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.61	0.26

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
TEAE ≤ CTCAE Grade 2
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	118 (87.4)	276 (96.8)
Number of Subjects Censored, n (%)	17 (12.6)	9 (3.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.07 (0.03, 0.13)	0.07 (0.07, 0.10)
Median (95% CI)	0.49 (0.33, 0.69)	0.30 (0.23, 0.39)
75% percentile (95% CI)	0.72 (0.69, 1.15)	0.69 (NE, NE)
Min, Max	0.0, 4.6*	0.0, 5.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.304 (0.113)
95% CI		(1.046, 1.626)
Log-rank p-value		0.028

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
TEAE ≤ CTCAE Grade 2
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	11.6 (6.0, 17.2)	3.2 (1.0, 5.4)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.49	0.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
TEAE ≥ CTCAE Grade 3
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	6 (42.9)	16 (80.0)
Number of Subjects Censored, n (%)	8 (57.1)	4 (20.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.39, NE)	0.66 (0.03, 1.35)
Median (95% CI)	NE (0.69, NE)	1.49 (0.62, 2.69)
75% percentile (95% CI)	NE (NE, NE)	2.69 (1.61, NE)
Min, Max	0.4, 2.9*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.576 (0.503)
95% CI		(0.588, 4.226)
Log-rank p-value		0.507

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
TEAE ≥ CTCAE Grade 3
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	NE (NE, NE)	23.3 (4.1, 42.5)
6 months	NE (NE, NE)	11.7 (0.0, 30.5)
9 months	NE (NE, NE)	11.7 (0.0, 30.5)
12 months	NE (NE, NE)	11.7 (0.0, 30.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.87	1.49

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
TEAE ≥ CTCAE Grade 3
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	33 (43.4)	90 (64.3)
Number of Subjects Censored, n (%)	43 (56.6)	50 (35.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.25 (0.69, 1.81)	0.95 (0.53, 1.28)
Median (95% CI)	5.55 (1.87, NE)	2.69 (1.71, 3.84)
75% percentile (95% CI)	NE (5.55, NE)	7.33 (5.98, NE)
Min, Max	0.2, 6.8*	0.1, 12.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.400 (0.210)
95% CI		(0.927, 2.114)
Log-rank p-value		0.100

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
TEAE ≥ CTCAE Grade 3
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	59.7 (48.5, 70.9)	46.9 (38.4, 55.3)
6 months	43.4 (25.0, 61.8)	33.0 (23.5, 42.4)
9 months	NE (NE, NE)	19.8 (7.5, 32.2)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.30	2.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
TEAE ≥ CTCAE Grade 3
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	59 (43.7)	166 (58.2)
Number of Subjects Censored, n (%)	76 (56.3)	119 (41.8)
Time to first TEAE (months)		
25% percentile (95% CI)	1.02 (0.72, 1.87)	0.95 (0.69, 1.31)
Median (95% CI)	4.14 (3.35, NE)	3.35 (2.56, 4.99)
75% percentile (95% CI)	9.26 (4.83, NE)	11.04 (7.46, NE)
Min, Max	0.1, 9.3	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.143 (0.155)
95% CI		(0.844, 1.549)
Log-rank p-value		0.259

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
TEAE ≥ CTCAE Grade 3
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	61.5 (53.2, 69.9)	51.6 (45.7, 57.5)
6 months	30.5 (9.2, 51.8)	38.8 (32.2, 45.4)
9 months	30.5 (9.2, 51.8)	28.7 (20.5, 36.9)
12 months	0.0 (NE, NE)	24.6 (14.4, 34.9)
18 months	0.0 (NE, NE)	16.4 (1.6, 31.2)
Median Follow-up Time (months)	2.69	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
Discontinuation due to TEAE
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	2 (14.3)	5 (25.0)
Number of Subjects Censored, n (%)	12 (85.7)	15 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.39, NE)	9.69 (0.30, NE)
Median (95% CI)	NE (NE, NE)	NE (9.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (9.69, NE)
Min, Max	0.4, 4.1*	0.3, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.083 (0.923)
95% CI		(0.178, 6.604)
Log-rank p-value		0.992

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
Discontinuation due to TEAE
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.1 (66.0, 100.0)	79.7 (61.9, 97.5)
6 months	NE (NE, NE)	79.7 (61.9, 97.5)
9 months	NE (NE, NE)	79.7 (61.9, 97.5)
12 months	NE (NE, NE)	53.1 (9.0, 97.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
Discontinuation due to TEAE
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	13 (17.1)	25 (17.9)
Number of Subjects Censored, n (%)	63 (82.9)	115 (82.1)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (3.65, NE)	8.28 (4.76, NE)
Median (95% CI)	NE (4.34, NE)	NE (8.90, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.1, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.735 (0.360)
95% CI		(0.363, 1.490)
Log-rank p-value		0.450

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
Discontinuation due to TEAE
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.3 (78.4, 94.2)	89.1 (83.8, 94.3)
6 months	69.4 (50.8, 87.9)	80.6 (72.5, 88.7)
9 months	NE (NE, NE)	65.2 (48.9, 81.4)
12 months	NE (NE, NE)	65.2 (48.9, 81.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
Discontinuation due to TEAE
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	23 (17.0)	52 (18.2)
Number of Subjects Censored, n (%)	112 (83.0)	233 (81.8)
Time to first TEAE (months)		
25% percentile (95% CI)	4.83 (3.15, NE)	8.21 (5.72, NE)
Median (95% CI)	NE (4.83, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.667 (0.264)
95% CI		(0.397, 1.119)
Log-rank p-value		0.162

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
Discontinuation due to TEAE
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.4 (78.1, 90.8)	87.8 (83.9, 91.6)
6 months	69.0 (50.8, 87.2)	80.7 (75.2, 86.1)
9 months	69.0 (50.8, 87.2)	72.0 (63.8, 80.2)
12 months	69.0 (50.8, 87.2)	66.9 (54.5, 79.2)
18 months	NE (NE, NE)	66.9 (54.5, 79.2)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
Deaths (Grade 5 TEAEs)
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Number of Subjects with Events, n (%)	0	4 (20.0)
Number of Subjects Censored, n (%)	14 (100.0)	16 (80.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	9.69 (0.62, NE)
Median (95% CI)	NE (NE, NE)	NE (3.02, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (9.69, NE)
Min, Max	0.9*, 4.1*	0.6, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.111

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
Deaths (Grade 5 TEAEs)
< 18.5

Statistics	Placebo + BSC N=14	Fruquintinib + BSC N=20
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	89.1 (74.7, 100.0)
6 months	NE (NE, NE)	80.2 (59.1, 100.0)
9 months	NE (NE, NE)	80.2 (59.1, 100.0)
12 months	NE (NE, NE)	53.4 (8.4, 98.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
Deaths (Grade 5 TEAEs)
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Number of Subjects with Events, n (%)	8 (10.5)	7 (5.0)
Number of Subjects Censored, n (%)	68 (89.5)	133 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.98, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.8*, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.395 (0.542)
95% CI		(0.136, 1.141)
Log-rank p-value		0.072

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
Deaths (Grade 5 TEAEs)
>= 18.5 to < 24

Statistics	Placebo + BSC N=76	Fruquintinib + BSC N=140
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.9 (82.8, 97.1)	96.3 (93.1, 99.5)
6 months	83.9 (70.8, 97.1)	94.8 (90.6, 99.1)
9 months	NE (NE, NE)	92.0 (85.2, 98.8)
12 months	NE (NE, NE)	92.0 (85.2, 98.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.2.3S
Summary of Time to Onset of Overall TEAE Excluding Disease Related Events by Body Mass Index
Safety Population
Deaths (Grade 5 TEAEs)
>= 24

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Number of Subjects with Events, n (%)	8 (5.9)	8 (2.8)
Number of Subjects Censored, n (%)	127 (94.1)	277 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 13.0*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.218 (0.564)
95% CI		(0.072, 0.657)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.
Disease-related AE(PT) are: Disease progression, Malignant neoplasm progression, Neoplasm progression, Colorectal cancer metastatic, Tumor pain, Tumor invasion, Metastasis, Metastases to meninges, Metastases to liver, Metastases to central nervous system, Cancer pain, Lung cancer metastatic.

Table 35.1.1.5.1.3C
Summary of Time to Onset of Overall TEAE by Sex
Safety Population
Deaths (Grade 5 TEAEs)
Female

Statistics	Placebo + BSC N=135	Fruquintinib + BSC N=285
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (88.2, 97.7)	98.9 (97.7, 100.0)
6 months	92.9 (88.2, 97.7)	96.6 (93.8, 99.5)
9 months	92.9 (88.2, 97.7)	93.8 (88.8, 98.7)
12 months	92.9 (88.2, 97.7)	93.8 (88.8, 98.7)
18 months	NE (NE, NE)	93.8 (88.8, 98.7)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	55 (46.6)	163 (66.8)
Number of Subjects Censored, n (%)	63 (53.4)	81 (33.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.72 (0.59, 1.22)	0.67 (0.43, 0.69)
Median (95% CI)	3.71 (1.87, NE)	1.61 (1.35, 2.63)
75% percentile (95% CI)	NE (NE, NE)	6.93 (4.70, NE)
Min, Max	0.0, 6.8*	0.0, 10.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.466 (0.159)
95% CI		(1.073, 2.001)
Log-rank p-value		0.023

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	54.0 (44.7, 63.4)	42.2 (35.9, 48.5)
6 months	43.1 (28.4, 57.7)	26.5 (19.7, 33.4)
9 months	NE (NE, NE)	18.4 (10.0, 26.8)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.89	1.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	19 (16.1)	67 (27.5)
Number of Subjects Censored, n (%)	99 (83.9)	177 (72.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.70, NE)	2.60 (1.05, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.609 (0.263)
95% CI		(0.961, 2.692)
Log-rank p-value		0.075

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.0 (77.1, 90.9)	74.0 (68.5, 79.6)
6 months	76.3 (60.8, 91.9)	71.0 (64.8, 77.1)
9 months	NE (NE, NE)	69.6 (63.0, 76.2)
12 months	NE (NE, NE)	69.6 (63.0, 76.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.78	2.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	17 (14.4)	50 (20.5)
Number of Subjects Censored, n (%)	101 (85.6)	194 (79.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.65, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.294 (0.285)
95% CI		(0.741, 2.261)
Log-rank p-value		0.379

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.8 (78.1, 91.5)	81.7 (76.8, 86.7)
6 months	84.8 (78.1, 91.5)	77.2 (71.4, 83.1)
9 months	NE (NE, NE)	75.3 (68.4, 82.1)
12 months	NE (NE, NE)	75.3 (68.4, 82.1)
18 months	NE (NE, NE)	75.3 (68.4, 82.1)
Median Follow-up Time (months)	2.78	3.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	12 (10.2)	31 (12.7)
Number of Subjects Censored, n (%)	106 (89.8)	213 (87.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.70, NE)	11.53 (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.028 (0.349)
95% CI		(0.518, 2.039)
Log-rank p-value		0.954

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.3 (83.1, 95.4)	90.0 (86.2, 93.8)
6 months	81.8 (66.8, 96.9)	86.9 (82.1, 91.6)
9 months	NE (NE, NE)	84.3 (78.5, 90.1)
12 months	NE (NE, NE)	70.2 (44.6, 95.8)
18 months	NE (NE, NE)	70.2 (44.6, 95.8)
Median Follow-up Time (months)	2.83	3.48

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	1 (0.8)	22 (9.0)
Number of Subjects Censored, n (%)	117 (99.2)	222 (91.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
Median (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.24, NE)
Min, Max	0.2*, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		10.185 (1.026)
95% CI		(1.363, 76.130)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.2, 100.0)	92.1 (88.7, 95.5)
6 months	99.0 (97.2, 100.0)	91.4 (87.7, 95.0)
9 months	NE (NE, NE)	89.0 (83.2, 94.8)
12 months	NE (NE, NE)	89.0 (83.2, 94.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.63

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	13 (11.0)	14 (5.7)
Number of Subjects Censored, n (%)	105 (89.0)	230 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	12.22 (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.349 (0.402)
95% CI		(0.159, 0.766)
Log-rank p-value		0.007

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.6 (82.5, 94.8)	96.5 (94.1, 98.9)
6 months	85.9 (78.0, 93.8)	92.7 (88.8, 96.7)
9 months	NE (NE, NE)	92.7 (88.8, 96.7)
12 months	NE (NE, NE)	92.7 (88.8, 96.7)
18 months	NE (NE, NE)	74.2 (41.5, 100.0)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	5 (4.2)	10 (4.1)
Number of Subjects Censored, n (%)	113 (95.8)	234 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.99, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.844 (0.561)
95% CI		(0.281, 2.533)
Log-rank p-value		0.738

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.2 (91.0, 99.4)	96.1 (93.6, 98.6)
6 months	95.2 (91.0, 99.4)	96.1 (93.6, 98.6)
9 months	NE (NE, NE)	96.1 (93.6, 98.6)
12 months	NE (NE, NE)	89.2 (76.0, 100.0)
18 months	NE (NE, NE)	89.2 (76.0, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	0	9 (3.7)
Number of Subjects Censored, n (%)	118 (100.0)	235 (96.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.00, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.229

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.8 (97.4, 100.0)
6 months	100.0 (100.0, 100.0)	96.3 (93.3, 99.4)
9 months	NE (NE, NE)	93.9 (88.4, 99.5)
12 months	NE (NE, NE)	83.7 (69.2, 98.2)
18 months	NE (NE, NE)	83.7 (69.2, 98.2)
Median Follow-up Time (months)	2.83	4.16

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	1 (0.8)	5 (2.0)
Number of Subjects Censored, n (%)	117 (99.2)	239 (98.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.488 (1.138)
95% CI		(0.160, 13.852)
Log-rank p-value		0.749

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.9, 100.0)	99.2 (98.0, 100.0)
6 months	98.9 (96.9, 100.0)	97.5 (94.9, 100.0)
9 months	NE (NE, NE)	95.1 (89.7, 100.0)
12 months	NE (NE, NE)	95.1 (89.7, 100.0)
18 months	NE (NE, NE)	95.1 (89.7, 100.0)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	1 (0.8)	6 (2.5)
Number of Subjects Censored, n (%)	117 (99.2)	238 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.500 (1.131)
95% CI		(0.163, 13.761)
Log-rank p-value		0.694

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.5, 100.0)	98.8 (97.4, 100.0)
6 months	99.1 (97.5, 100.0)	96.7 (93.5, 99.9)
9 months	NE (NE, NE)	93.1 (85.6, 100.0)
12 months	NE (NE, NE)	93.1 (85.6, 100.0)
18 months	NE (NE, NE)	93.1 (85.6, 100.0)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	68 (57.6)	163 (66.8)
Number of Subjects Censored, n (%)	50 (42.4)	81 (33.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.56 (0.30, 0.69)	0.57 (0.39, 0.69)
Median (95% CI)	1.61 (0.95, 3.75)	1.45 (0.95, 2.37)
75% percentile (95% CI)	NE (4.34, NE)	7.62 (4.90, NE)
Min, Max	0.0, 6.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.027 (0.149)
95% CI		(0.767, 1.374)
Log-rank p-value		0.756

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	41.2 (31.9, 50.5)	39.5 (33.2, 45.8)
6 months	31.8 (18.1, 45.5)	25.4 (18.0, 32.7)
9 months	NE (NE, NE)	19.2 (10.9, 27.4)
12 months	NE (NE, NE)	14.4 (4.1, 24.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.30	1.31

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	11 (9.3)	54 (22.1)
Number of Subjects Censored, n (%)	107 (90.7)	190 (77.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.95 (2.37, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.158 (0.334)
95% CI		(1.122, 4.151)
Log-rank p-value		0.017

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.2 (84.7, 95.7)	79.7 (74.6, 84.9)
6 months	90.2 (84.7, 95.7)	74.5 (67.8, 81.1)
9 months	NE (NE, NE)	73.0 (65.9, 80.1)
12 months	NE (NE, NE)	73.0 (65.9, 80.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	23 (19.5)	41 (16.8)
Number of Subjects Censored, n (%)	95 (80.5)	203 (83.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.77, NE)	9.00 (5.55, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.609 (0.274)
95% CI		(0.356, 1.042)
Log-rank p-value		0.069

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.5 (73.1, 87.9)	85.6 (80.9, 90.3)
6 months	75.5 (63.7, 87.3)	79.9 (73.6, 86.2)
9 months	NE (NE, NE)	77.0 (69.8, 84.3)
12 months	NE (NE, NE)	73.0 (62.6, 83.3)
18 months	NE (NE, NE)	73.0 (62.6, 83.3)
Median Follow-up Time (months)	2.78	3.10

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	20 (16.9)	46 (18.9)
Number of Subjects Censored, n (%)	98 (83.1)	198 (81.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.53, NE)	7.75 (4.21, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.827 (0.282)
95% CI		(0.476, 1.438)
Log-rank p-value		0.671

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.6 (75.4, 89.8)	85.0 (80.2, 89.7)
6 months	78.0 (67.0, 89.1)	78.1 (71.8, 84.5)
9 months	NE (NE, NE)	72.3 (63.5, 81.1)
12 months	NE (NE, NE)	66.7 (53.5, 80.0)
18 months	NE (NE, NE)	66.7 (53.5, 80.0)
Median Follow-up Time (months)	2.78	3.19

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	11 (9.3)	49 (20.1)
Number of Subjects Censored, n (%)	107 (90.7)	195 (79.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	7.10 (3.02, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.647 (0.338)
95% CI		(0.849, 3.194)
Log-rank p-value		0.136

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.2 (84.6, 95.7)	81.3 (76.1, 86.4)
6 months	90.2 (84.6, 95.7)	76.5 (70.1, 83.0)
9 months	NE (NE, NE)	74.6 (67.2, 81.9)
12 months	NE (NE, NE)	70.2 (59.3, 81.0)
18 months	NE (NE, NE)	70.2 (59.3, 81.0)
Median Follow-up Time (months)	2.83	2.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	16 (13.6)	35 (14.3)
Number of Subjects Censored, n (%)	102 (86.4)	209 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	18.04 (6.21, NE)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.1, 6.8*	0.0, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.727 (0.312)
95% CI		(0.394, 1.339)
Log-rank p-value		0.329

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.5 (78.9, 92.1)	90.1 (86.2, 94.0)
6 months	85.5 (78.9, 92.1)	83.3 (77.4, 89.1)
9 months	NE (NE, NE)	78.6 (71.1, 86.2)
12 months	NE (NE, NE)	78.6 (71.1, 86.2)
18 months	NE (NE, NE)	78.6 (71.1, 86.2)
Median Follow-up Time (months)	2.83	3.40

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	5 (4.2)	40 (16.4)
Number of Subjects Censored, n (%)	113 (95.8)	204 (83.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.87, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.381 (0.528)
95% CI		(1.555, 12.341)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (91.4, 99.3)	85.4 (80.9, 89.9)
6 months	95.4 (91.4, 99.3)	82.9 (77.8, 88.1)
9 months	NE (NE, NE)	78.8 (71.3, 86.2)
12 months	NE (NE, NE)	78.8 (71.3, 86.2)
18 months	NE (NE, NE)	78.8 (71.3, 86.2)
Median Follow-up Time (months)	2.83	3.07

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	1 (0.8)	22 (9.0)
Number of Subjects Censored, n (%)	117 (99.2)	222 (91.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		9.267 (1.028)
95% CI		(1.237, 69.437)
Log-rank p-value		0.010

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.4, 100.0)	92.8 (89.5, 96.1)
6 months	99.1 (97.4, 100.0)	89.4 (84.8, 94.0)
9 months	NE (NE, NE)	87.0 (80.5, 93.5)
12 months	NE (NE, NE)	87.0 (80.5, 93.5)
18 months	NE (NE, NE)	87.0 (80.5, 93.5)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	2 (1.7)	9 (3.7)
Number of Subjects Censored, n (%)	116 (98.3)	235 (96.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.6, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.701 (0.797)
95% CI		(0.357, 8.114)
Log-rank p-value		0.488

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (95.7, 100.0)	97.1 (95.0, 99.2)
6 months	98.2 (95.7, 100.0)	96.3 (93.6, 98.9)
9 months	NE (NE, NE)	93.9 (88.7, 99.1)
12 months	NE (NE, NE)	93.9 (88.7, 99.1)
18 months	NE (NE, NE)	93.9 (88.7, 99.1)
Median Follow-up Time (months)	2.83	4.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	3 (2.5)	4 (1.6)
Number of Subjects Censored, n (%)	115 (97.5)	240 (98.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.449 (0.781)
95% CI		(0.097, 2.073)
Log-rank p-value		0.399

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.0 (93.6, 100.0)	98.1 (96.2, 100.0)
6 months	97.0 (93.6, 100.0)	98.1 (96.2, 100.0)
9 months	NE (NE, NE)	98.1 (96.2, 100.0)
12 months	NE (NE, NE)	98.1 (96.2, 100.0)
18 months	NE (NE, NE)	98.1 (96.2, 100.0)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	6 (5.1)	1 (0.4)
Number of Subjects Censored, n (%)	112 (94.9)	243 (99.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.045 (1.200)
95% CI		(0.004, 0.467)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.5 (90.2, 98.8)	100.0 (100.0, 100.0)
6 months	94.5 (90.2, 98.8)	98.8 (96.3, 100.0)
9 months	NE (NE, NE)	98.8 (96.3, 100.0)
12 months	NE (NE, NE)	98.8 (96.3, 100.0)
18 months	NE (NE, NE)	98.8 (96.3, 100.0)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	0	4 (1.6)
Number of Subjects Censored, n (%)	118 (100.0)	240 (98.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.116

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.3 (96.6, 100.0)
6 months	100.0 (100.0, 100.0)	98.3 (96.6, 100.0)
9 months	NE (NE, NE)	98.3 (96.6, 100.0)
12 months	NE (NE, NE)	98.3 (96.6, 100.0)
18 months	NE (NE, NE)	98.3 (96.6, 100.0)
Median Follow-up Time (months)	2.83	4.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	22 (18.6)	97 (39.8)
Number of Subjects Censored, n (%)	96 (81.4)	147 (60.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.54, NE)	1.61 (0.95, 1.87)
Median (95% CI)	NE (NE, NE)	NE (5.68, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.021 (0.243)
95% CI		(1.255, 3.254)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.8 (74.8, 88.9)	63.9 (57.7, 70.1)
6 months	77.0 (65.7, 88.3)	57.0 (49.8, 64.2)
9 months	NE (NE, NE)	50.6 (41.5, 59.6)
12 months	NE (NE, NE)	50.6 (41.5, 59.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	12 (10.2)	57 (23.4)
Number of Subjects Censored, n (%)	106 (89.8)	187 (76.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.27, NE)	5.36 (2.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.144 (0.332)
95% CI		(1.118, 4.113)
Log-rank p-value		0.021

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.2 (84.7, 95.7)	78.7 (73.4, 83.9)
6 months	85.2 (74.4, 96.1)	74.3 (68.0, 80.5)
9 months	NE (NE, NE)	71.0 (63.5, 78.5)
12 months	NE (NE, NE)	71.0 (63.5, 78.5)
18 months	NE (NE, NE)	71.0 (63.5, 78.5)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	2 (1.7)	15 (6.1)
Number of Subjects Censored, n (%)	116 (98.3)	229 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.688 (0.761)
95% CI		(0.605, 11.939)
Log-rank p-value		0.150

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (96.0, 100.0)	94.6 (91.6, 97.6)
6 months	98.3 (96.0, 100.0)	93.0 (89.4, 96.7)
9 months	NE (NE, NE)	90.7 (85.0, 96.4)
12 months	NE (NE, NE)	90.7 (85.0, 96.4)
18 months	NE (NE, NE)	90.7 (85.0, 96.4)
Median Follow-up Time (months)	2.83	3.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	1 (0.8)	11 (4.5)
Number of Subjects Censored, n (%)	117 (99.2)	233 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.224 (1.059)
95% CI		(0.405, 25.698)
Log-rank p-value		0.251

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.4, 100.0)	96.9 (94.6, 99.2)
6 months	99.1 (97.4, 100.0)	93.9 (89.9, 97.9)
9 months	NE (NE, NE)	91.8 (86.0, 97.5)
12 months	NE (NE, NE)	91.8 (86.0, 97.5)
18 months	NE (NE, NE)	91.8 (86.0, 97.5)
Median Follow-up Time (months)	2.83	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	2 (1.7)	6 (2.5)
Number of Subjects Censored, n (%)	116 (98.3)	238 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.212 (0.832)
95% CI		(0.237, 6.184)
Log-rank p-value		0.838

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (95.9, 100.0)	97.9 (96.0, 99.7)
6 months	98.3 (95.9, 100.0)	97.1 (94.8, 99.5)
9 months	NE (NE, NE)	97.1 (94.8, 99.5)
12 months	NE (NE, NE)	97.1 (94.8, 99.5)
18 months	NE (NE, NE)	97.1 (94.8, 99.5)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	3 (2.5)	8 (3.3)
Number of Subjects Censored, n (%)	115 (97.5)	236 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.130 (0.684)
95% CI		(0.296, 4.315)
Log-rank p-value		0.849

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (94.6, 100.0)	96.9 (94.6, 99.2)
6 months	97.4 (94.6, 100.0)	95.8 (92.7, 98.9)
9 months	NE (NE, NE)	95.8 (92.7, 98.9)
12 months	NE (NE, NE)	95.8 (92.7, 98.9)
18 months	NE (NE, NE)	95.8 (92.7, 98.9)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	0	9 (3.7)
Number of Subjects Censored, n (%)	118 (100.0)	235 (96.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.6, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.080

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.0 (94.9, 99.2)
6 months	100.0 (100.0, 100.0)	95.8 (92.6, 99.0)
9 months	NE (NE, NE)	93.8 (88.7, 98.8)
12 months	NE (NE, NE)	93.8 (88.7, 98.8)
18 months	NE (NE, NE)	93.8 (88.7, 98.8)
Median Follow-up Time (months)	2.83	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	1 (0.8)	8 (3.3)
Number of Subjects Censored, n (%)	117 (99.2)	236 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.087 (1.067)
95% CI		(0.381, 24.986)
Log-rank p-value		0.301

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.5, 100.0)	96.4 (94.0, 98.9)
6 months	99.1 (97.5, 100.0)	96.4 (94.0, 98.9)
9 months	NE (NE, NE)	96.4 (94.0, 98.9)
12 months	NE (NE, NE)	96.4 (94.0, 98.9)
18 months	NE (NE, NE)	96.4 (94.0, 98.9)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	2 (1.7)	8 (3.3)
Number of Subjects Censored, n (%)	116 (98.3)	236 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.583 (0.800)
95% CI		(0.330, 7.587)
Log-rank p-value		0.530

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (95.9, 100.0)	97.0 (94.7, 99.2)
6 months	98.3 (95.9, 100.0)	97.0 (94.7, 99.2)
9 months	NE (NE, NE)	95.6 (92.3, 99.0)
12 months	NE (NE, NE)	95.6 (92.3, 99.0)
18 months	NE (NE, NE)	95.6 (92.3, 99.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	0	6 (2.5)
Number of Subjects Censored, n (%)	118 (100.0)	238 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.079

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.5 (95.5, 99.5)
6 months	100.0 (100.0, 100.0)	97.5 (95.5, 99.5)
9 months	NE (NE, NE)	97.5 (95.5, 99.5)
12 months	NE (NE, NE)	97.5 (95.5, 99.5)
18 months	NE (NE, NE)	97.5 (95.5, 99.5)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	0	7 (2.9)
Number of Subjects Censored, n (%)	118 (100.0)	237 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.166

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.4 (96.7, 100.0)
6 months	100.0 (100.0, 100.0)	95.2 (91.6, 98.8)
9 months	NE (NE, NE)	95.2 (91.6, 98.8)
12 months	NE (NE, NE)	95.2 (91.6, 98.8)
18 months	NE (NE, NE)	95.2 (91.6, 98.8)
Median Follow-up Time (months)	2.83	3.98

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	33 (28.0)	94 (38.5)
Number of Subjects Censored, n (%)	85 (72.0)	150 (61.5)
Time to first TEAE (months)		
25% percentile (95% CI)	1.77 (0.92, NE)	1.58 (0.95, 1.97)
Median (95% CI)	NE (5.82, NE)	NE (6.05, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.200 (0.205)
95% CI		(0.803, 1.794)
Log-rank p-value		0.344

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.6 (64.3, 80.9)	64.9 (58.8, 71.0)
6 months	55.7 (30.0, 81.3)	58.6 (51.4, 65.8)
9 months	NE (NE, NE)	52.2 (43.4, 61.0)
12 months	NE (NE, NE)	52.2 (43.4, 61.0)
18 months	NE (NE, NE)	52.2 (43.4, 61.0)
Median Follow-up Time (months)	2.78	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	9 (7.6)	32 (13.1)
Number of Subjects Censored, n (%)	109 (92.4)	212 (86.9)
Time to first TEAE (months)		
25% percentile (95% CI)	5.82 (5.82, NE)	NE (6.87, NE)
Median (95% CI)	NE (5.82, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.293 (0.386)
95% CI		(0.607, 2.754)
Log-rank p-value		0.459

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.7 (86.0, 97.3)	89.3 (85.4, 93.3)
6 months	73.3 (40.9, 100.0)	84.7 (79.1, 90.2)
9 months	NE (NE, NE)	81.5 (74.7, 88.4)
12 months	NE (NE, NE)	81.5 (74.7, 88.4)
18 months	NE (NE, NE)	81.5 (74.7, 88.4)
Median Follow-up Time (months)	2.83	3.40

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	6 (5.1)	34 (13.9)
Number of Subjects Censored, n (%)	112 (94.9)	210 (86.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.457 (0.447)
95% CI		(1.022, 5.905)
Log-rank p-value		0.044

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.8 (90.7, 98.8)	86.3 (81.7, 90.8)
6 months	94.8 (90.7, 98.8)	83.6 (78.2, 89.0)
9 months	NE (NE, NE)	83.6 (78.2, 89.0)
12 months	NE (NE, NE)	83.6 (78.2, 89.0)
18 months	NE (NE, NE)	83.6 (78.2, 89.0)
Median Follow-up Time (months)	2.83	3.48

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	6 (5.1)	32 (13.1)
Number of Subjects Censored, n (%)	112 (94.9)	212 (86.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.313 (0.450)
95% CI		(0.957, 5.590)
Log-rank p-value		0.059

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.8 (90.8, 98.9)	88.3 (84.1, 92.5)
6 months	94.8 (90.8, 98.9)	85.2 (80.2, 90.2)
9 months	NE (NE, NE)	83.8 (78.2, 89.5)
12 months	NE (NE, NE)	83.8 (78.2, 89.5)
18 months	NE (NE, NE)	83.8 (78.2, 89.5)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	6 (5.1)	21 (8.6)
Number of Subjects Censored, n (%)	112 (94.9)	223 (91.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.381 (0.467)
95% CI		(0.553, 3.451)
Log-rank p-value		0.585

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (90.8, 98.9)	92.6 (89.3, 96.0)
6 months	94.9 (90.8, 98.9)	89.3 (84.8, 93.9)
9 months	NE (NE, NE)	89.3 (84.8, 93.9)
12 months	NE (NE, NE)	89.3 (84.8, 93.9)
18 months	NE (NE, NE)	89.3 (84.8, 93.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	1 (0.8)	11 (4.5)
Number of Subjects Censored, n (%)	117 (99.2)	233 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.880 (1.059)
95% CI		(0.487, 30.934)
Log-rank p-value		0.154

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.4, 100.0)	96.5 (94.0, 98.9)
6 months	99.1 (97.4, 100.0)	95.5 (92.4, 98.5)
9 months	NE (NE, NE)	92.9 (88.2, 97.5)
12 months	NE (NE, NE)	92.9 (88.2, 97.5)
18 months	NE (NE, NE)	92.9 (88.2, 97.5)
Median Follow-up Time (months)	2.83	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	4 (3.4)	17 (7.0)
Number of Subjects Censored, n (%)	114 (96.6)	227 (93.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.652 (0.565)
95% CI		(0.546, 4.998)
Log-rank p-value		0.394

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.6 (93.3, 99.9)	93.5 (90.3, 96.7)
6 months	96.6 (93.3, 99.9)	91.3 (87.0, 95.7)
9 months	NE (NE, NE)	91.3 (87.0, 95.7)
12 months	NE (NE, NE)	91.3 (87.0, 95.7)
18 months	NE (NE, NE)	91.3 (87.0, 95.7)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	1 (0.8)	12 (4.9)
Number of Subjects Censored, n (%)	117 (99.2)	232 (95.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.785 (1.045)
95% CI		(0.617, 37.096)
Log-rank p-value		0.099

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.5, 100.0)	95.7 (93.1, 98.3)
6 months	99.2 (97.5, 100.0)	93.9 (90.4, 97.5)
9 months	NE (NE, NE)	93.9 (90.4, 97.5)
12 months	NE (NE, NE)	93.9 (90.4, 97.5)
18 months	NE (NE, NE)	93.9 (90.4, 97.5)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	3 (2.5)	8 (3.3)
Number of Subjects Censored, n (%)	115 (97.5)	236 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.112 (0.683)
95% CI		(0.291, 4.239)
Log-rank p-value		0.883

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (93.9, 100.0)	97.0 (94.8, 99.2)
6 months	97.1 (93.9, 100.0)	96.1 (93.3, 98.9)
9 months	NE (NE, NE)	96.1 (93.3, 98.9)
12 months	NE (NE, NE)	96.1 (93.3, 98.9)
18 months	NE (NE, NE)	96.1 (93.3, 98.9)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	1 (0.8)	8 (3.3)
Number of Subjects Censored, n (%)	117 (99.2)	236 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.569 (1.078)
95% CI		(0.311, 21.246)
Log-rank p-value		0.375

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.4, 100.0)	97.2 (95.0, 99.5)
6 months	99.1 (97.4, 100.0)	96.3 (93.5, 99.2)
9 months	NE (NE, NE)	94.4 (89.8, 99.1)
12 months	NE (NE, NE)	94.4 (89.8, 99.1)
18 months	NE (NE, NE)	94.4 (89.8, 99.1)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	2 (1.7)	6 (2.5)
Number of Subjects Censored, n (%)	116 (98.3)	238 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.975 (0.838)
95% CI		(0.189, 5.041)
Log-rank p-value		0.964

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (95.9, 100.0)	97.8 (95.9, 99.7)
6 months	98.3 (95.9, 100.0)	97.8 (95.9, 99.7)
9 months	NE (NE, NE)	95.8 (91.6, 100.0)
12 months	NE (NE, NE)	95.8 (91.6, 100.0)
18 months	NE (NE, NE)	95.8 (91.6, 100.0)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	32 (27.1)	95 (38.9)
Number of Subjects Censored, n (%)	86 (72.9)	149 (61.1)
Time to first TEAE (months)		
25% percentile (95% CI)	1.84 (0.95, NE)	0.72 (0.69, 1.84)
Median (95% CI)	NE (NE, NE)	9.69 (6.41, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.293 (0.208)
95% CI		(0.859, 1.945)
Log-rank p-value		0.251

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.0 (62.4, 79.6)	65.8 (59.8, 71.8)
6 months	71.0 (62.4, 79.6)	60.0 (53.1, 66.9)
9 months	NE (NE, NE)	54.4 (46.0, 62.7)
12 months	NE (NE, NE)	39.5 (19.7, 59.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.33	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	7 (5.9)	38 (15.6)
Number of Subjects Censored, n (%)	111 (94.1)	206 (84.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.699 (0.413)
95% CI		(1.201, 6.068)
Log-rank p-value		0.012

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.4 (88.5, 98.2)	84.6 (80.0, 89.2)
6 months	93.4 (88.5, 98.2)	83.9 (79.1, 88.6)
9 months	NE (NE, NE)	83.9 (79.1, 88.6)
12 months	NE (NE, NE)	83.9 (79.1, 88.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.10

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	12 (10.2)	21 (8.6)
Number of Subjects Censored, n (%)	106 (89.8)	223 (91.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	14.32 (10.28, NE)
Median (95% CI)	NE (NE, NE)	NE (14.32, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (14.32, NE)
Min, Max	0.0, 6.8*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.595 (0.377)
95% CI		(0.284, 1.247)
Log-rank p-value		0.173

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.4 (83.7, 95.1)	93.4 (90.1, 96.6)
6 months	89.4 (83.7, 95.1)	90.8 (86.5, 95.1)
9 months	NE (NE, NE)	89.5 (84.6, 94.5)
12 months	NE (NE, NE)	82.1 (67.3, 96.8)
18 months	NE (NE, NE)	54.7 (9.8, 99.6)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	13 (11.0)	25 (10.2)
Number of Subjects Censored, n (%)	105 (89.0)	219 (89.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.670 (0.354)
95% CI		(0.335, 1.342)
Log-rank p-value		0.263

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.2 (82.2, 94.3)	91.0 (87.3, 94.7)
6 months	88.2 (82.2, 94.3)	89.4 (85.1, 93.6)
9 months	NE (NE, NE)	88.0 (83.1, 93.0)
12 months	NE (NE, NE)	75.4 (52.2, 98.7)
18 months	NE (NE, NE)	75.4 (52.2, 98.7)
Median Follow-up Time (months)	2.76	3.48

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	2 (1.7)	11 (4.5)
Number of Subjects Censored, n (%)	116 (98.3)	233 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.575 (0.772)
95% CI		(0.567, 11.694)
Log-rank p-value		0.230

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (95.9, 100.0)	95.3 (92.6, 98.0)
6 months	98.3 (95.9, 100.0)	95.3 (92.6, 98.0)
9 months	NE (NE, NE)	95.3 (92.6, 98.0)
12 months	NE (NE, NE)	95.3 (92.6, 98.0)
18 months	NE (NE, NE)	95.3 (92.6, 98.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	2 (1.7)	9 (3.7)
Number of Subjects Censored, n (%)	116 (98.3)	235 (96.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.384 (0.808)
95% CI		(0.284, 6.746)
Log-rank p-value		0.785

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (95.5, 100.0)	97.5 (95.6, 99.5)
6 months	98.1 (95.5, 100.0)	96.5 (93.8, 99.3)
9 months	NE (NE, NE)	93.2 (87.9, 98.5)
12 months	NE (NE, NE)	93.2 (87.9, 98.5)
18 months	NE (NE, NE)	93.2 (87.9, 98.5)
Median Follow-up Time (months)	2.83	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Vascular disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	15 (12.7)	102 (41.8)
Number of Subjects Censored, n (%)	103 (87.3)	142 (58.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.89 (0.69, 1.45)
Median (95% CI)	NE (NE, NE)	NE (4.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.667 (0.278)
95% CI		(2.127, 6.324)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Vascular disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.1 (79.5, 92.7)	58.4 (52.0, 64.8)
6 months	86.1 (79.5, 92.7)	56.7 (50.1, 63.3)
9 months	NE (NE, NE)	53.5 (45.9, 61.1)
12 months	NE (NE, NE)	53.5 (45.9, 61.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.78	2.69

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	9 (7.6)	95 (38.9)
Number of Subjects Censored, n (%)	109 (92.4)	149 (61.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.95 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	NE (6.93, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.804 (0.350)
95% CI		(2.923, 11.526)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.4 (85.9, 96.9)	61.0 (54.7, 67.3)
6 months	91.4 (85.9, 96.9)	60.3 (53.9, 66.7)
9 months	NE (NE, NE)	56.9 (49.4, 64.5)
12 months	NE (NE, NE)	56.9 (49.4, 64.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	24 (20.3)	83 (34.0)
Number of Subjects Censored, n (%)	94 (79.7)	161 (66.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.35, NE)	1.68 (1.02, 2.56)
Median (95% CI)	NE (NE, NE)	NE (9.76, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.580 (0.239)
95% CI		(0.990, 2.523)
Log-rank p-value		0.045

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.5 (71.9, 87.1)	67.5 (61.5, 73.6)
6 months	75.9 (65.9, 85.9)	62.5 (55.5, 69.6)
9 months	NE (NE, NE)	60.8 (53.2, 68.5)
12 months	NE (NE, NE)	54.8 (41.5, 68.0)
18 months	NE (NE, NE)	54.8 (41.5, 68.0)
Median Follow-up Time (months)	2.64	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	8 (6.8)	29 (11.9)
Number of Subjects Censored, n (%)	110 (93.2)	215 (88.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.569 (0.428)
95% CI		(0.678, 3.627)
Log-rank p-value		0.288

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (88.2, 97.7)	89.4 (85.3, 93.4)
6 months	92.9 (88.2, 97.7)	86.0 (81.0, 91.1)
9 months	NE (NE, NE)	84.8 (79.2, 90.4)
12 months	NE (NE, NE)	84.8 (79.2, 90.4)
18 months	NE (NE, NE)	84.8 (79.2, 90.4)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	5 (4.2)	30 (12.3)
Number of Subjects Censored, n (%)	113 (95.8)	214 (87.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.98, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.279 (0.489)
95% CI		(0.874, 5.940)
Log-rank p-value		0.092

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (91.8, 99.4)	89.6 (85.7, 93.6)
6 months	95.6 (91.8, 99.4)	85.6 (80.1, 91.1)
9 months	NE (NE, NE)	81.1 (73.0, 89.2)
12 months	NE (NE, NE)	81.1 (73.0, 89.2)
18 months	NE (NE, NE)	81.1 (73.0, 89.2)
Median Follow-up Time (months)	2.83	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	3 (2.5)	10 (4.1)
Number of Subjects Censored, n (%)	115 (97.5)	234 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.442 (0.671)
95% CI		(0.387, 5.370)
Log-rank p-value		0.505

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (95.9, 100.0)	96.2 (93.8, 98.6)
6 months	94.5 (86.9, 100.0)	95.2 (92.0, 98.3)
9 months	NE (NE, NE)	95.2 (92.0, 98.3)
12 months	NE (NE, NE)	95.2 (92.0, 98.3)
18 months	NE (NE, NE)	95.2 (92.0, 98.3)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	4 (3.4)	9 (3.7)
Number of Subjects Censored, n (%)	114 (96.6)	235 (96.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.747 (0.618)
95% CI		(0.222, 2.509)
Log-rank p-value		0.637

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.5 (93.1, 99.9)	96.6 (94.3, 98.9)
6 months	96.5 (93.1, 99.9)	95.3 (92.0, 98.7)
9 months	NE (NE, NE)	95.3 (92.0, 98.7)
12 months	NE (NE, NE)	95.3 (92.0, 98.7)
18 months	NE (NE, NE)	95.3 (92.0, 98.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	0	6 (2.5)
Number of Subjects Censored, n (%)	118 (100.0)	238 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.223

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.7 (97.3, 100.0)
6 months	100.0 (100.0, 100.0)	97.6 (94.9, 100.0)
9 months	NE (NE, NE)	93.5 (87.3, 99.7)
12 months	NE (NE, NE)	93.5 (87.3, 99.7)
18 months	NE (NE, NE)	93.5 (87.3, 99.7)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	0	10 (4.1)
Number of Subjects Censored, n (%)	118 (100.0)	234 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.041

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.6 (92.9, 98.3)
6 months	100.0 (100.0, 100.0)	95.6 (92.9, 98.3)
9 months	NE (NE, NE)	95.6 (92.9, 98.3)
12 months	NE (NE, NE)	95.6 (92.9, 98.3)
18 months	NE (NE, NE)	95.6 (92.9, 98.3)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	15 (12.7)	95 (38.9)
Number of Subjects Censored, n (%)	103 (87.3)	149 (61.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	1.38 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	13.14 (6.24, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.14, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.383 (0.289)
95% CI		(1.920, 5.961)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.8 (81.7, 93.8)	63.3 (57.1, 69.5)
6 months	83.4 (73.2, 93.5)	59.0 (52.1, 65.8)
9 months	NE (NE, NE)	55.3 (47.0, 63.5)
12 months	NE (NE, NE)	55.3 (47.0, 63.5)
18 months	NE (NE, NE)	27.6 (0.0, 66.1)
Median Follow-up Time (months)	2.79	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	5 (4.2)	52 (21.3)
Number of Subjects Censored, n (%)	113 (95.8)	192 (78.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	7.39 (2.46, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.040 (0.521)
95% CI		(2.176, 16.764)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (91.9, 99.4)	80.3 (75.3, 85.4)
6 months	95.6 (91.9, 99.4)	77.0 (71.1, 82.8)
9 months	NE (NE, NE)	74.7 (67.6, 81.8)
12 months	NE (NE, NE)	74.7 (67.6, 81.8)
18 months	NE (NE, NE)	74.7 (67.6, 81.8)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	5 (4.2)	13 (5.3)
Number of Subjects Censored, n (%)	113 (95.8)	231 (94.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.034 (0.533)
95% CI		(0.364, 2.938)
Log-rank p-value		0.963

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (92.0, 99.4)	94.3 (91.3, 97.4)
6 months	95.7 (92.0, 99.4)	94.3 (91.3, 97.4)
9 months	NE (NE, NE)	94.3 (91.3, 97.4)
12 months	NE (NE, NE)	94.3 (91.3, 97.4)
18 months	NE (NE, NE)	94.3 (91.3, 97.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	3 (2.5)	7 (2.9)
Number of Subjects Censored, n (%)	115 (97.5)	237 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.896 (0.704)
95% CI		(0.226, 3.560)
Log-rank p-value		0.921

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (95.6, 100.0)	97.4 (95.4, 99.5)
6 months	94.2 (86.3, 100.0)	96.7 (94.2, 99.2)
9 months	NE (NE, NE)	96.7 (94.2, 99.2)
12 months	NE (NE, NE)	96.7 (94.2, 99.2)
18 months	NE (NE, NE)	96.7 (94.2, 99.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Nervous system disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	19 (16.1)	60 (24.6)
Number of Subjects Censored, n (%)	99 (83.9)	184 (75.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.91, NE)	4.86 (2.56, NE)
Median (95% CI)	NE (NE, NE)	18.04 (11.10, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.279 (0.268)
95% CI		(0.756, 2.163)
Log-rank p-value		0.451

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Nervous system disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.1 (76.1, 90.1)	79.8 (74.7, 85.0)
6 months	83.1 (76.1, 90.1)	72.5 (65.7, 79.3)
9 months	NE (NE, NE)	69.9 (62.4, 77.3)
12 months	NE (NE, NE)	59.9 (40.7, 79.1)
18 months	NE (NE, NE)	59.9 (40.7, 79.1)
Median Follow-up Time (months)	2.73	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	8 (6.8)	23 (9.4)
Number of Subjects Censored, n (%)	110 (93.2)	221 (90.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.1, 6.8*	0.1, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.184 (0.419)
95% CI		(0.521, 2.690)
Log-rank p-value		0.752

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.5 (87.4, 97.6)	92.1 (88.7, 95.5)
6 months	92.5 (87.4, 97.6)	91.2 (87.3, 95.0)
9 months	NE (NE, NE)	88.5 (83.3, 93.7)
12 months	NE (NE, NE)	88.5 (83.3, 93.7)
18 months	NE (NE, NE)	88.5 (83.3, 93.7)
Median Follow-up Time (months)	2.83	3.40

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	2 (1.7)	4 (1.6)
Number of Subjects Censored, n (%)	116 (98.3)	240 (98.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.778 (0.882)
95% CI		(0.138, 4.388)
Log-rank p-value		0.715

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (96.0, 100.0)	98.3 (96.7, 100.0)
6 months	98.3 (96.0, 100.0)	98.3 (96.7, 100.0)
9 months	NE (NE, NE)	98.3 (96.7, 100.0)
12 months	NE (NE, NE)	98.3 (96.7, 100.0)
18 months	NE (NE, NE)	98.3 (96.7, 100.0)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	1 (0.8)	6 (2.5)
Number of Subjects Censored, n (%)	117 (99.2)	238 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.910 (1.084)
95% CI		(0.348, 24.354)
Log-rank p-value		0.339

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.4, 100.0)	97.5 (95.6, 99.5)
6 months	99.1 (97.4, 100.0)	97.5 (95.6, 99.5)
9 months	NE (NE, NE)	97.5 (95.6, 99.5)
12 months	NE (NE, NE)	97.5 (95.6, 99.5)
18 months	NE (NE, NE)	97.5 (95.6, 99.5)
Median Follow-up Time (months)	2.83	4.16

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	11 (9.3)	55 (22.5)
Number of Subjects Censored, n (%)	107 (90.7)	189 (77.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	5.78 (3.35, NE)
Median (95% CI)	NE (NE, NE)	13.60 (13.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.2*, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.842 (0.336)
95% CI		(0.953, 3.561)
Log-rank p-value		0.068

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.0 (85.6, 96.3)	82.1 (77.1, 87.0)
6 months	87.0 (77.8, 96.2)	73.9 (67.3, 80.6)
9 months	NE (NE, NE)	70.6 (62.8, 78.4)
12 months	NE (NE, NE)	70.6 (62.8, 78.4)
18 months	NE (NE, NE)	47.1 (9.1, 85.1)
Median Follow-up Time (months)	2.83	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	5 (4.2)	40 (16.4)
Number of Subjects Censored, n (%)	113 (95.8)	204 (83.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.60 (5.06, NE)
Median (95% CI)	NE (NE, NE)	NE (13.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.2*, 6.8*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.891 (0.480)
95% CI		(1.129, 7.404)
Log-rank p-value		0.021

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (91.9, 99.4)	86.9 (82.5, 91.3)
6 months	95.7 (91.9, 99.4)	80.2 (74.1, 86.4)
9 months	NE (NE, NE)	78.4 (71.4, 85.4)
12 months	NE (NE, NE)	78.4 (71.4, 85.4)
18 months	NE (NE, NE)	52.3 (10.2, 94.3)
Median Follow-up Time (months)	2.83	3.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	1 (0.8)	4 (1.6)
Number of Subjects Censored, n (%)	117 (99.2)	240 (98.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.028 (1.145)
95% CI		(0.109, 9.692)
Log-rank p-value		0.941

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.5, 100.0)	98.7 (97.3, 100.0)
6 months	99.1 (97.5, 100.0)	97.9 (95.8, 100.0)
9 months	NE (NE, NE)	97.9 (95.8, 100.0)
12 months	NE (NE, NE)	97.9 (95.8, 100.0)
18 months	NE (NE, NE)	97.9 (95.8, 100.0)
Median Follow-up Time (months)	2.83	4.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Infections and infestations**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	16 (13.6)	59 (24.2)
Number of Subjects Censored, n (%)	102 (86.4)	185 (75.8)
Time to first TEAE (months)		
25% percentile (95% CI)	5.78 (4.34, NE)	5.52 (3.52, 6.87)
Median (95% CI)	NE (5.78, NE)	11.53 (7.92, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Min, Max	0.0, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.294 (0.299)
95% CI		(0.720, 2.324)
Log-rank p-value		0.356

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Infections and infestations**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.6 (81.4, 93.7)	82.2 (77.1, 87.3)
6 months	65.9 (35.6, 96.2)	70.8 (63.2, 78.3)
9 months	NE (NE, NE)	57.3 (45.6, 69.0)
12 months	NE (NE, NE)	45.8 (23.7, 68.0)
18 months	NE (NE, NE)	45.8 (23.7, 68.0)
Median Follow-up Time (months)	2.83	2.91

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	4 (3.4)	8 (3.3)
Number of Subjects Censored, n (%)	114 (96.6)	236 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.14, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.543 (0.646)
95% CI		(0.153, 1.929)
Log-rank p-value		0.578

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (96.0, 100.0)	97.4 (95.4, 99.5)
6 months	88.0 (74.2, 100.0)	95.0 (91.1, 98.9)
9 months	NE (NE, NE)	95.0 (91.1, 98.9)
12 months	NE (NE, NE)	95.0 (91.1, 98.9)
18 months	NE (NE, NE)	95.0 (91.1, 98.9)
Median Follow-up Time (months)	2.83	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	1 (0.8)	10 (4.1)
Number of Subjects Censored, n (%)	117 (99.2)	234 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (11.56, NE)
Median (95% CI)	NE (NE, NE)	NE (11.56, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.253 (1.072)
95% CI		(0.276, 18.412)
Log-rank p-value		0.435

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.1 (96.3, 100.0)
6 months	94.7 (84.7, 100.0)	94.7 (90.9, 98.5)
9 months	NE (NE, NE)	93.1 (88.4, 97.9)
12 months	NE (NE, NE)	79.8 (55.3, 100.0)
18 months	NE (NE, NE)	79.8 (55.3, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	1 (0.8)	6 (2.5)
Number of Subjects Censored, n (%)	117 (99.2)	238 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.940 (1.090)
95% CI		(0.229, 16.445)
Log-rank p-value		0.565

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.5, 100.0)	97.5 (95.3, 99.7)
6 months	99.1 (97.5, 100.0)	96.3 (93.2, 99.5)
9 months	NE (NE, NE)	96.3 (93.2, 99.5)
12 months	NE (NE, NE)	96.3 (93.2, 99.5)
18 months	NE (NE, NE)	96.3 (93.2, 99.5)
Median Follow-up Time (months)	2.83	4.16

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	15 (12.7)	33 (13.5)
Number of Subjects Censored, n (%)	103 (87.3)	211 (86.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.47, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.839 (0.321)
95% CI		(0.447, 1.574)
Log-rank p-value		0.638

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.4 (79.9, 92.8)	89.0 (84.9, 93.1)
6 months	86.4 (79.9, 92.8)	83.2 (77.2, 89.2)
9 months	NE (NE, NE)	80.1 (73.0, 87.3)
12 months	NE (NE, NE)	80.1 (73.0, 87.3)
18 months	NE (NE, NE)	80.1 (73.0, 87.3)
Median Follow-up Time (months)	2.83	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	11 (9.3)	17 (7.0)
Number of Subjects Censored, n (%)	107 (90.7)	227 (93.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.517 (0.405)
95% CI		(0.233, 1.143)
Log-rank p-value		0.119

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.7 (83.9, 95.5)	95.6 (92.8, 98.3)
6 months	89.7 (83.9, 95.5)	89.6 (84.1, 95.0)
9 months	NE (NE, NE)	88.2 (82.3, 94.1)
12 months	NE (NE, NE)	88.2 (82.3, 94.1)
18 months	NE (NE, NE)	88.2 (82.3, 94.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	1 (0.8)	12 (4.9)
Number of Subjects Censored, n (%)	117 (99.2)	232 (95.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.006 (1.042)
95% CI		(0.779, 46.309)
Log-rank p-value		0.053

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.5, 100.0)	94.8 (91.8, 97.7)
6 months	99.1 (97.5, 100.0)	94.8 (91.8, 97.7)
9 months	NE (NE, NE)	94.8 (91.8, 97.7)
12 months	NE (NE, NE)	94.8 (91.8, 97.7)
18 months	NE (NE, NE)	94.8 (91.8, 97.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Endocrine disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	0	51 (20.9)
Number of Subjects Censored, n (%)	118 (100.0)	193 (79.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.98 (3.84, NE)
Median (95% CI)	NE (NE, NE)	NE (9.33, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Endocrine disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	83.3 (78.5, 88.2)
6 months	100.0 (100.0, 100.0)	73.9 (66.5, 81.3)
9 months	NE (NE, NE)	69.1 (60.4, 77.8)
12 months	NE (NE, NE)	63.3 (49.9, 76.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	0	47 (19.3)
Number of Subjects Censored, n (%)	118 (100.0)	197 (80.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	6.47 (5.52, NE)
Median (95% CI)	NE (NE, NE)	NE (9.33, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	85.1 (80.5, 89.8)
6 months	100.0 (100.0, 100.0)	76.7 (69.7, 83.8)
9 months	NE (NE, NE)	69.8 (60.5, 79.0)
12 months	NE (NE, NE)	64.4 (51.2, 77.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Psychiatric disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	10 (8.5)	30 (12.3)
Number of Subjects Censored, n (%)	108 (91.5)	214 (87.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.145 (0.371)
95% CI		(0.553, 2.367)
Log-rank p-value		0.653

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Psychiatric disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.8 (85.4, 96.3)	88.0 (83.5, 92.4)
6 months	90.8 (85.4, 96.3)	85.6 (80.6, 90.6)
9 months	NE (NE, NE)	84.0 (78.1, 89.8)
12 months	NE (NE, NE)	84.0 (78.1, 89.8)
18 months	NE (NE, NE)	84.0 (78.1, 89.8)
Median Follow-up Time (months)	2.83	3.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	7 (5.9)	17 (7.0)
Number of Subjects Censored, n (%)	111 (94.1)	227 (93.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.833 (0.457)
95% CI		(0.340, 2.040)
Log-rank p-value		0.749

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.7 (89.1, 98.3)	93.4 (90.0, 96.8)
6 months	93.7 (89.1, 98.3)	91.7 (87.7, 95.7)
9 months	NE (NE, NE)	90.0 (84.9, 95.2)
12 months	NE (NE, NE)	90.0 (84.9, 95.2)
18 months	NE (NE, NE)	90.0 (84.9, 95.2)
Median Follow-up Time (months)	2.83	3.63

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	0	6 (2.5)
Number of Subjects Censored, n (%)	118 (100.0)	238 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.127

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.0 (94.6, 99.4)
6 months	100.0 (100.0, 100.0)	97.0 (94.6, 99.4)
9 months	NE (NE, NE)	97.0 (94.6, 99.4)
12 months	NE (NE, NE)	97.0 (94.6, 99.4)
18 months	NE (NE, NE)	97.0 (94.6, 99.4)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	2 (1.7)	3 (1.2)
Number of Subjects Censored, n (%)	116 (98.3)	241 (98.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.691 (0.919)
95% CI		(0.114, 4.182)
Log-rank p-value		0.736

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (95.2, 100.0)	98.7 (97.2, 100.0)
6 months	98.0 (95.2, 100.0)	98.7 (97.2, 100.0)
9 months	NE (NE, NE)	98.7 (97.2, 100.0)
12 months	NE (NE, NE)	98.7 (97.2, 100.0)
18 months	NE (NE, NE)	98.7 (97.2, 100.0)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	10 (8.5)	29 (11.9)
Number of Subjects Censored, n (%)	108 (91.5)	215 (88.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.018 (0.373)
95% CI		(0.490, 2.113)
Log-rank p-value		0.962

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.2 (86.0, 96.4)	89.3 (85.3, 93.4)
6 months	91.2 (86.0, 96.4)	85.5 (80.1, 90.9)
9 months	NE (NE, NE)	83.3 (76.6, 90.1)
12 months	NE (NE, NE)	83.3 (76.6, 90.1)
18 months	NE (NE, NE)	83.3 (76.6, 90.1)
Median Follow-up Time (months)	2.83	3.37

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	1 (0.8)	11 (4.5)
Number of Subjects Censored, n (%)	117 (99.2)	233 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.634 (1.048)
95% CI		(0.466, 28.330)
Log-rank p-value		0.188

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.0, 100.0)	95.4 (92.6, 98.2)
6 months	99.0 (97.0, 100.0)	94.2 (90.6, 97.8)
9 months	NE (NE, NE)	94.2 (90.6, 97.8)
12 months	NE (NE, NE)	94.2 (90.6, 97.8)
18 months	NE (NE, NE)	94.2 (90.6, 97.8)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Number of Subjects with Events, n (%)	0	10 (4.1)
Number of Subjects Censored, n (%)	118 (100.0)	234 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.072

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
<65 years

Statistics	Placebo + BSC N=118	Fruquintinib + BSC N=244
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.5 (94.2, 98.9)
6 months	100.0 (100.0, 100.0)	95.8 (93.0, 98.6)
9 months	NE (NE, NE)	93.5 (88.3, 98.7)
12 months	NE (NE, NE)	93.5 (88.3, 98.7)
18 months	NE (NE, NE)	93.5 (88.3, 98.7)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	74 (66.1)	152 (71.7)
Number of Subjects Censored, n (%)	38 (33.9)	60 (28.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.48 (0.16, 0.69)	0.28 (0.20, 0.43)
Median (95% CI)	1.28 (0.72, 1.87)	0.87 (0.69, 1.12)
75% percentile (95% CI)	NE (2.60, NE)	7.29 (3.25, NE)
Min, Max	0.0, 13.0*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.115 (0.144)
95% CI		(0.840, 1.479)
Log-rank p-value		0.529

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	32.7 (23.6, 41.8)	32.7 (26.3, 39.2)
6 months	29.1 (18.6, 39.6)	25.3 (18.8, 31.8)
9 months	29.1 (18.6, 39.6)	23.0 (15.7, 30.3)
12 months	29.1 (18.6, 39.6)	23.0 (15.7, 30.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.26	0.87

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	33 (29.5)	88 (41.5)
Number of Subjects Censored, n (%)	79 (70.5)	124 (58.5)
Time to first TEAE (months)		
25% percentile (95% CI)	1.84 (0.69, NE)	0.72 (0.69, 1.18)
Median (95% CI)	NE (NE, NE)	NE (3.52, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.376 (0.207)
95% CI		(0.916, 2.065)
Log-rank p-value		0.127

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	69.7 (60.8, 78.6)	60.5 (53.7, 67.3)
6 months	65.6 (54.1, 77.0)	55.7 (48.4, 63.0)
9 months	65.6 (54.1, 77.0)	52.0 (42.2, 61.8)
12 months	65.6 (54.1, 77.0)	52.0 (42.2, 61.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.22	2.69

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	20 (17.9)	41 (19.3)
Number of Subjects Censored, n (%)	92 (82.1)	171 (80.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.64, NE)	NE (5.55, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.047 (0.278)
95% CI		(0.607, 1.805)
Log-rank p-value		0.867

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.5 (72.7, 88.3)	81.2 (75.8, 86.5)
6 months	80.5 (72.7, 88.3)	79.8 (73.9, 85.7)
9 months	80.5 (72.7, 88.3)	77.7 (70.6, 84.7)
12 months	80.5 (72.7, 88.3)	77.7 (70.6, 84.7)
18 months	NE (NE, NE)	77.7 (70.6, 84.7)
Median Follow-up Time (months)	2.41	3.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	11 (9.8)	15 (7.1)
Number of Subjects Censored, n (%)	101 (90.2)	197 (92.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.626 (0.407)
95% CI		(0.282, 1.390)
Log-rank p-value		0.217

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.5 (83.5, 95.4)	93.5 (90.0, 96.9)
6 months	89.5 (83.5, 95.4)	91.3 (86.8, 95.9)
9 months	89.5 (83.5, 95.4)	91.3 (86.8, 95.9)
12 months	89.5 (83.5, 95.4)	91.3 (86.8, 95.9)
18 months	NE (NE, NE)	91.3 (86.8, 95.9)
Median Follow-up Time (months)	2.76	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	5 (4.5)	40 (18.9)
Number of Subjects Censored, n (%)	107 (95.5)	172 (81.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.71, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.817 (0.477)
95% CI		(1.499, 9.720)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.2 (91.1, 99.3)	82.5 (77.3, 87.7)
6 months	95.2 (91.1, 99.3)	79.7 (73.8, 85.7)
9 months	95.2 (91.1, 99.3)	77.5 (70.2, 84.7)
12 months	95.2 (91.1, 99.3)	77.5 (70.2, 84.7)
18 months	NE (NE, NE)	77.5 (70.2, 84.7)
Median Follow-up Time (months)	2.79	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	15 (13.4)	13 (6.1)
Number of Subjects Censored, n (%)	97 (86.6)	199 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.310 (0.398)
95% CI		(0.142, 0.678)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.6 (78.5, 92.7)	95.5 (92.7, 98.4)
6 months	80.8 (69.6, 92.1)	91.1 (85.9, 96.2)
9 months	80.8 (69.6, 92.1)	91.1 (85.9, 96.2)
12 months	80.8 (69.6, 92.1)	91.1 (85.9, 96.2)
18 months	NE (NE, NE)	91.1 (85.9, 96.2)
Median Follow-up Time (months)	2.79	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	12 (10.7)	12 (5.7)
Number of Subjects Censored, n (%)	100 (89.3)	200 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.415 (0.421)
95% CI		(0.182, 0.946)
Log-rank p-value		0.029

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (83.0, 94.8)	94.6 (91.6, 97.7)
6 months	88.9 (83.0, 94.8)	94.6 (91.6, 97.7)
9 months	88.9 (83.0, 94.8)	91.0 (83.4, 98.6)
12 months	88.9 (83.0, 94.8)	91.0 (83.4, 98.6)
18 months	NE (NE, NE)	91.0 (83.4, 98.6)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	5 (4.5)	7 (3.3)
Number of Subjects Censored, n (%)	107 (95.5)	205 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.611 (0.614)
95% CI		(0.183, 2.039)
Log-rank p-value		0.333

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.2 (91.0, 99.3)	97.5 (95.3, 99.7)
6 months	95.2 (91.0, 99.3)	96.7 (94.0, 99.3)
9 months	95.2 (91.0, 99.3)	96.7 (94.0, 99.3)
12 months	95.2 (91.0, 99.3)	92.1 (82.9, 100.0)
18 months	NE (NE, NE)	92.1 (82.9, 100.0)
Median Follow-up Time (months)	2.79	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	3 (2.7)	6 (2.8)
Number of Subjects Censored, n (%)	109 (97.3)	206 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.910 (0.710)
95% CI		(0.226, 3.661)
Log-rank p-value		0.931

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.4 (92.2, 100.0)	96.7 (94.1, 99.3)
6 months	96.4 (92.2, 100.0)	96.7 (94.1, 99.3)
9 months	96.4 (92.2, 100.0)	96.7 (94.1, 99.3)
12 months	96.4 (92.2, 100.0)	96.7 (94.1, 99.3)
18 months	NE (NE, NE)	96.7 (94.1, 99.3)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	1 (0.9)	5 (2.4)
Number of Subjects Censored, n (%)	111 (99.1)	207 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.679 (1.099)
95% CI		(0.311, 23.111)
Log-rank p-value		0.351

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.3, 100.0)	97.6 (95.5, 99.7)
6 months	99.1 (97.3, 100.0)	97.6 (95.5, 99.7)
9 months	99.1 (97.3, 100.0)	97.6 (95.5, 99.7)
12 months	99.1 (97.3, 100.0)	97.6 (95.5, 99.7)
18 months	NE (NE, NE)	97.6 (95.5, 99.7)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	63 (56.3)	146 (68.9)
Number of Subjects Censored, n (%)	49 (43.8)	66 (31.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.56 (0.26, 0.72)	0.49 (0.39, 0.69)
Median (95% CI)	1.84 (1.22, 3.35)	1.51 (0.95, 1.91)
75% percentile (95% CI)	5.36 (3.35, NE)	6.47 (3.71, NE)
Min, Max	0.0, 5.6*	0.0, 11.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.088 (0.154)
95% CI		(0.804, 1.471)
Log-rank p-value		0.488

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	41.0 (30.3, 51.7)	37.8 (31.1, 44.5)
6 months	NE (NE, NE)	25.3 (18.1, 32.5)
9 months	NE (NE, NE)	19.7 (11.8, 27.7)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.38	1.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	13 (11.6)	56 (26.4)
Number of Subjects Censored, n (%)	99 (88.4)	156 (73.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.88 (1.84, 6.70)
Median (95% CI)	NE (NE, NE)	NE (10.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.991 (0.314)
95% CI		(1.077, 3.682)
Log-rank p-value		0.027

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.1 (82.1, 94.2)	78.6 (72.9, 84.3)
6 months	88.1 (82.1, 94.2)	69.7 (61.8, 77.6)
9 months	88.1 (82.1, 94.2)	63.6 (53.8, 73.4)
12 months	88.1 (82.1, 94.2)	56.5 (40.8, 72.3)
18 months	NE (NE, NE)	56.5 (40.8, 72.3)
Median Follow-up Time (months)	2.56	2.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	19 (17.0)	38 (17.9)
Number of Subjects Censored, n (%)	93 (83.0)	174 (82.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.79, NE)	9.20 (5.03, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.825 (0.290)
95% CI		(0.467, 1.457)
Log-rank p-value		0.559

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.0 (74.5, 89.5)	84.7 (79.7, 89.7)
6 months	82.0 (74.5, 89.5)	79.5 (72.9, 86.0)
9 months	82.0 (74.5, 89.5)	76.7 (68.5, 85.0)
12 months	82.0 (74.5, 89.5)	73.1 (62.6, 83.6)
18 months	NE (NE, NE)	73.1 (62.6, 83.6)
Median Follow-up Time (months)	2.51	3.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	17 (15.2)	37 (17.5)
Number of Subjects Censored, n (%)	95 (84.8)	175 (82.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.92, NE)	12.25 (6.18, NE)
Median (95% CI)	NE (NE, NE)	NE (12.25, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.897 (0.302)
95% CI		(0.496, 1.623)
Log-rank p-value		0.749

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.5 (72.5, 90.5)	84.9 (79.8, 89.9)
6 months	81.5 (72.5, 90.5)	82.5 (76.9, 88.1)
9 months	81.5 (72.5, 90.5)	79.1 (72.1, 86.2)
12 months	81.5 (72.5, 90.5)	75.2 (65.1, 85.3)
18 months	NE (NE, NE)	60.1 (32.6, 87.7)
Median Follow-up Time (months)	2.79	3.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	11 (9.8)	29 (13.7)
Number of Subjects Censored, n (%)	101 (90.2)	183 (86.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.15, NE)	NE (6.70, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.008 (0.365)
95% CI		(0.493, 2.061)
Log-rank p-value		0.998

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.2 (80.0, 96.3)	90.0 (85.8, 94.2)
6 months	84.6 (74.3, 95.0)	83.6 (77.6, 89.7)
9 months	84.6 (74.3, 95.0)	79.3 (71.2, 87.5)
12 months	84.6 (74.3, 95.0)	79.3 (71.2, 87.5)
18 months	NE (NE, NE)	79.3 (71.2, 87.5)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	12 (10.7)	31 (14.6)
Number of Subjects Censored, n (%)	100 (89.3)	181 (85.4)
Time to first TEAE (months)		
25% percentile (95% CI)	5.36 (3.52, NE)	10.18 (7.39, NE)
Median (95% CI)	NE (5.36, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.031 (0.350)
95% CI		(0.520, 2.047)
Log-rank p-value		0.985

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.2 (84.4, 96.0)	87.7 (83.1, 92.2)
6 months	71.0 (44.0, 98.0)	84.1 (78.2, 90.1)
9 months	71.0 (44.0, 98.0)	81.9 (74.6, 89.2)
12 months	71.0 (44.0, 98.0)	73.3 (60.1, 86.4)
18 months	NE (NE, NE)	73.3 (60.1, 86.4)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	3 (2.7)	27 (12.7)
Number of Subjects Censored, n (%)	109 (97.3)	185 (87.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.106 (0.613)
95% CI		(1.537, 16.963)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (93.8, 100.0)	88.0 (83.5, 92.4)
6 months	97.1 (93.8, 100.0)	86.0 (80.8, 91.1)
9 months	97.1 (93.8, 100.0)	86.0 (80.8, 91.1)
12 months	97.1 (93.8, 100.0)	86.0 (80.8, 91.1)
18 months	NE (NE, NE)	86.0 (80.8, 91.1)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	7 (6.3)	12 (5.7)
Number of Subjects Censored, n (%)	105 (93.8)	200 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.6, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.643 (0.493)
95% CI		(0.245, 1.688)
Log-rank p-value		0.379

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.3 (89.9, 98.8)	94.9 (91.8, 98.0)
6 months	78.6 (50.2, 100.0)	93.0 (88.9, 97.0)
9 months	NE (NE, NE)	93.0 (88.9, 97.0)
12 months	NE (NE, NE)	93.0 (88.9, 97.0)
18 months	NE (NE, NE)	93.0 (88.9, 97.0)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	2 (1.8)	7 (3.3)
Number of Subjects Censored, n (%)	110 (98.2)	205 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.538 (0.814)
95% CI		(0.312, 7.591)
Log-rank p-value		0.704

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (95.5, 100.0)	97.1 (94.9, 99.4)
6 months	98.1 (95.5, 100.0)	95.7 (92.0, 99.3)
9 months	98.1 (95.5, 100.0)	95.7 (92.0, 99.3)
12 months	98.1 (95.5, 100.0)	95.7 (92.0, 99.3)
18 months	NE (NE, NE)	95.7 (92.0, 99.3)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	1 (0.9)	7 (3.3)
Number of Subjects Censored, n (%)	111 (99.1)	205 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.226 (1.074)
95% CI		(0.393, 26.494)
Log-rank p-value		0.248

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.4, 100.0)	96.7 (94.3, 99.1)
6 months	99.1 (97.4, 100.0)	96.7 (94.3, 99.1)
9 months	99.1 (97.4, 100.0)	96.7 (94.3, 99.1)
12 months	99.1 (97.4, 100.0)	96.7 (94.3, 99.1)
18 months	NE (NE, NE)	96.7 (94.3, 99.1)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	5 (4.5)	2 (0.9)
Number of Subjects Censored, n (%)	107 (95.5)	210 (99.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.193 (0.838)
95% CI		(0.037, 0.997)
Log-rank p-value		0.038

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (91.0, 99.3)	99.0 (97.6, 100.0)
6 months	95.1 (91.0, 99.3)	99.0 (97.6, 100.0)
9 months	95.1 (91.0, 99.3)	99.0 (97.6, 100.0)
12 months	95.1 (91.0, 99.3)	99.0 (97.6, 100.0)
18 months	NE (NE, NE)	99.0 (97.6, 100.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	0	9 (4.2)
Number of Subjects Censored, n (%)	112 (100.0)	203 (95.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.041

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.9 (93.1, 98.7)
6 months	100.0 (100.0, 100.0)	95.9 (93.1, 98.7)
9 months	100.0 (100.0, 100.0)	93.3 (87.4, 99.1)
12 months	100.0 (100.0, 100.0)	93.3 (87.4, 99.1)
18 months	NE (NE, NE)	93.3 (87.4, 99.1)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	41 (36.6)	99 (46.7)
Number of Subjects Censored, n (%)	71 (63.4)	113 (53.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.99 (0.69, 1.87)	0.92 (0.69, 1.58)
Median (95% CI)	10.18 (3.22, NE)	5.55 (2.99, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.0, 10.2	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.112 (0.190)
95% CI		(0.767, 1.613)
Log-rank p-value		0.492

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	62.6 (53.0, 72.1)	56.2 (49.3, 63.2)
6 months	58.7 (47.1, 70.3)	49.1 (41.3, 56.9)
9 months	58.7 (47.1, 70.3)	46.1 (37.7, 54.5)
12 months	0.0 (NE, NE)	43.0 (33.3, 52.8)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	28 (25.0)	67 (31.6)
Number of Subjects Censored, n (%)	84 (75.0)	145 (68.4)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.92, NE)	2.53 (1.31, 3.09)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.185 (0.229)
95% CI		(0.756, 1.856)
Log-rank p-value		0.448

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.4 (64.9, 81.9)	69.3 (62.8, 75.9)
6 months	73.4 (64.9, 81.9)	66.3 (59.4, 73.2)
9 months	73.4 (64.9, 81.9)	64.8 (57.5, 72.1)
12 months	73.4 (64.9, 81.9)	61.7 (52.6, 70.8)
18 months	NE (NE, NE)	61.7 (52.6, 70.8)
Median Follow-up Time (months)	2.32	2.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	2 (1.8)	13 (6.1)
Number of Subjects Censored, n (%)	110 (98.2)	199 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.842 (0.764)
95% CI		(0.635, 12.710)
Log-rank p-value		0.157

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (95.6, 100.0)	93.3 (89.7, 96.8)
6 months	98.2 (95.6, 100.0)	93.3 (89.7, 96.8)
9 months	98.2 (95.6, 100.0)	93.3 (89.7, 96.8)
12 months	98.2 (95.6, 100.0)	93.3 (89.7, 96.8)
18 months	NE (NE, NE)	93.3 (89.7, 96.8)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	4 (3.6)	9 (4.2)
Number of Subjects Censored, n (%)	108 (96.4)	203 (95.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.926 (0.618)
95% CI		(0.276, 3.108)
Log-rank p-value		0.964

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (94.2, 100.0)	96.1 (93.4, 98.7)
6 months	93.4 (85.3, 100.0)	95.1 (91.9, 98.4)
9 months	93.4 (85.3, 100.0)	95.1 (91.9, 98.4)
12 months	93.4 (85.3, 100.0)	95.1 (91.9, 98.4)
18 months	NE (NE, NE)	95.1 (91.9, 98.4)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	2 (1.8)	8 (3.8)
Number of Subjects Censored, n (%)	110 (98.2)	204 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.524 (0.807)
95% CI		(0.314, 7.403)
Log-rank p-value		0.641

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (94.7, 100.0)	96.4 (93.7, 99.0)
6 months	97.8 (94.7, 100.0)	96.4 (93.7, 99.0)
9 months	97.8 (94.7, 100.0)	92.9 (85.8, 100.0)
12 months	97.8 (94.7, 100.0)	92.9 (85.8, 100.0)
18 months	NE (NE, NE)	92.9 (85.8, 100.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	0	7 (3.3)
Number of Subjects Censored, n (%)	112 (100.0)	205 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.118

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.0 (94.6, 99.4)
6 months	100.0 (100.0, 100.0)	97.0 (94.6, 99.4)
9 months	100.0 (100.0, 100.0)	94.6 (89.3, 99.8)
12 months	100.0 (100.0, 100.0)	94.6 (89.3, 99.8)
18 months	NE (NE, NE)	94.6 (89.3, 99.8)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	0	9 (4.2)
Number of Subjects Censored, n (%)	112 (100.0)	203 (95.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.044

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.5 (93.9, 99.1)
6 months	100.0 (100.0, 100.0)	94.6 (90.9, 98.2)
9 months	100.0 (100.0, 100.0)	94.6 (90.9, 98.2)
12 months	100.0 (100.0, 100.0)	94.6 (90.9, 98.2)
18 months	NE (NE, NE)	94.6 (90.9, 98.2)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	2 (1.8)	5 (2.4)
Number of Subjects Censored, n (%)	110 (98.2)	207 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.949 (0.864)
95% CI		(0.175, 5.155)
Log-rank p-value		0.997

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (93.2, 100.0)	98.1 (96.2, 99.9)
6 months	97.2 (93.2, 100.0)	98.1 (96.2, 99.9)
9 months	97.2 (93.2, 100.0)	96.4 (92.5, 100.0)
12 months	97.2 (93.2, 100.0)	96.4 (92.5, 100.0)
18 months	NE (NE, NE)	96.4 (92.5, 100.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	0	5 (2.4)
Number of Subjects Censored, n (%)	112 (100.0)	207 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.208

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.0 (97.7, 100.0)
6 months	100.0 (100.0, 100.0)	96.8 (93.4, 100.0)
9 months	100.0 (100.0, 100.0)	93.4 (85.9, 100.0)
12 months	100.0 (100.0, 100.0)	93.4 (85.9, 100.0)
18 months	NE (NE, NE)	93.4 (85.9, 100.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	3 (2.7)	5 (2.4)
Number of Subjects Censored, n (%)	109 (97.3)	207 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Median (95% CI)	10.18 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 10.2	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.672 (0.768)
95% CI		(0.149, 3.027)
Log-rank p-value		0.704

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (95.6, 100.0)	97.4 (95.1, 99.7)
6 months	98.2 (95.6, 100.0)	97.4 (95.1, 99.7)
9 months	98.2 (95.6, 100.0)	97.4 (95.1, 99.7)
12 months	0.0 (NE, NE)	97.4 (95.1, 99.7)
18 months	0.0 (NE, NE)	97.4 (95.1, 99.7)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	1 (0.9)	4 (1.9)
Number of Subjects Censored, n (%)	111 (99.1)	208 (98.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.036 (1.177)
95% CI		(0.103, 10.405)
Log-rank p-value		0.963

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (96.9, 100.0)	99.0 (97.7, 100.0)
6 months	99.0 (96.9, 100.0)	96.1 (91.8, 100.0)
9 months	99.0 (96.9, 100.0)	96.1 (91.8, 100.0)
12 months	99.0 (96.9, 100.0)	96.1 (91.8, 100.0)
18 months	NE (NE, NE)	96.1 (91.8, 100.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	30 (26.8)	92 (43.4)
Number of Subjects Censored, n (%)	82 (73.2)	120 (56.6)
Time to first TEAE (months)		
25% percentile (95% CI)	2.17 (0.95, 5.59)	1.61 (0.95, 1.91)
Median (95% CI)	5.59 (3.55, NE)	6.47 (5.49, NE)
75% percentile (95% CI)	NE (5.59, NE)	NE (16.79, NE)
Min, Max	0.4*, 6.5*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.404 (0.216)
95% CI		(0.920, 2.143)
Log-rank p-value		0.166

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.8 (64.0, 81.5)	60.9 (54.1, 67.8)
6 months	49.1 (19.0, 79.3)	52.8 (44.7, 60.8)
9 months	NE (NE, NE)	44.7 (35.1, 54.3)
12 months	NE (NE, NE)	44.7 (35.1, 54.3)
18 months	NE (NE, NE)	29.8 (5.1, 54.5)
Median Follow-up Time (months)	2.43	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	12 (10.7)	24 (11.3)
Number of Subjects Censored, n (%)	100 (89.3)	188 (88.7)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.845 (0.366)
95% CI		(0.412, 1.730)
Log-rank p-value		0.435

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.0 (81.2, 94.8)	89.2 (84.8, 93.6)
6 months	73.3 (46.5, 100.0)	86.9 (81.5, 92.3)
9 months	NE (NE, NE)	84.5 (77.5, 91.5)
12 months	NE (NE, NE)	84.5 (77.5, 91.5)
18 months	NE (NE, NE)	84.5 (77.5, 91.5)
Median Follow-up Time (months)	2.73	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	5 (4.5)	14 (6.6)
Number of Subjects Censored, n (%)	107 (95.5)	198 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.842 (0.563)
95% CI		(0.279, 2.538)
Log-rank p-value		0.553

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.3 (92.8, 99.9)	96.1 (93.5, 98.8)
6 months	80.3 (51.4, 100.0)	92.8 (88.3, 97.4)
9 months	NE (NE, NE)	86.8 (78.9, 94.7)
12 months	NE (NE, NE)	86.8 (78.9, 94.7)
18 months	NE (NE, NE)	86.8 (78.9, 94.7)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	3 (2.7)	15 (7.1)
Number of Subjects Censored, n (%)	109 (97.3)	197 (92.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.648 (0.661)
95% CI		(0.451, 6.025)
Log-rank p-value		0.614

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (95.6, 100.0)	95.0 (91.9, 98.0)
6 months	81.8 (52.4, 100.0)	92.6 (88.1, 97.1)
9 months	NE (NE, NE)	86.5 (78.5, 94.5)
12 months	NE (NE, NE)	86.5 (78.5, 94.5)
18 months	NE (NE, NE)	86.5 (78.5, 94.5)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	5 (4.5)	15 (7.1)
Number of Subjects Censored, n (%)	107 (95.5)	197 (92.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.162 (0.530)
95% CI		(0.411, 3.282)
Log-rank p-value		0.805

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (91.5, 99.3)	95.0 (91.9, 98.0)
6 months	95.4 (91.5, 99.3)	92.4 (88.3, 96.5)
9 months	95.4 (91.5, 99.3)	88.3 (81.4, 95.1)
12 months	95.4 (91.5, 99.3)	88.3 (81.4, 95.1)
18 months	NE (NE, NE)	88.3 (81.4, 95.1)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	2 (1.8)	21 (9.9)
Number of Subjects Censored, n (%)	110 (98.2)	191 (90.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (8.51, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.148 (0.752)
95% CI		(1.180, 22.461)
Log-rank p-value		0.025

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.2, 100.0)	90.3 (86.2, 94.5)
6 months	92.9 (81.6, 100.0)	88.8 (83.6, 93.9)
9 months	92.9 (81.6, 100.0)	85.3 (77.1, 93.5)
12 months	92.9 (81.6, 100.0)	85.3 (77.1, 93.5)
18 months	NE (NE, NE)	85.3 (77.1, 93.5)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	6 (5.4)	7 (3.3)
Number of Subjects Censored, n (%)	106 (94.6)	205 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.417 (0.589)
95% CI		(0.131, 1.323)
Log-rank p-value		0.135

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.4 (88.2, 98.6)	97.5 (95.3, 99.7)
6 months	93.4 (88.2, 98.6)	96.6 (93.7, 99.4)
9 months	93.4 (88.2, 98.6)	94.9 (90.6, 99.2)
12 months	93.4 (88.2, 98.6)	94.9 (90.6, 99.2)
18 months	NE (NE, NE)	94.9 (90.6, 99.2)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	1 (0.9)	15 (7.1)
Number of Subjects Censored, n (%)	111 (99.1)	197 (92.9)
Time to first TEAE (months)		
25% percentile (95% CI)	7.43 (7.43, NE)	NE (NE, NE)
Median (95% CI)	NE (7.43, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (7.43, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.865 (1.038)
95% CI		(0.767, 44.839)
Log-rank p-value		0.056

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	92.9 (89.3, 96.5)
6 months	100.0 (100.0, 100.0)	91.9 (87.9, 96.0)
9 months	NE (NE, NE)	91.9 (87.9, 96.0)
12 months	NE (NE, NE)	91.9 (87.9, 96.0)
18 months	NE (NE, NE)	91.9 (87.9, 96.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	2 (1.8)	12 (5.7)
Number of Subjects Censored, n (%)	110 (98.2)	200 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.55, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.052 (0.778)
95% CI		(0.446, 9.438)
Log-rank p-value		0.334

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.2, 100.0)	95.2 (92.2, 98.3)
6 months	93.2 (82.5, 100.0)	93.0 (88.6, 97.4)
9 months	93.2 (82.5, 100.0)	91.4 (86.0, 96.7)
12 months	93.2 (82.5, 100.0)	91.4 (86.0, 96.7)
18 months	NE (NE, NE)	91.4 (86.0, 96.7)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	0	5 (2.4)
Number of Subjects Censored, n (%)	112 (100.0)	207 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.089

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.3 (94.9, 99.6)
6 months	100.0 (100.0, 100.0)	97.3 (94.9, 99.6)
9 months	100.0 (100.0, 100.0)	97.3 (94.9, 99.6)
12 months	100.0 (100.0, 100.0)	97.3 (94.9, 99.6)
18 months	NE (NE, NE)	97.3 (94.9, 99.6)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	0	5 (2.4)
Number of Subjects Censored, n (%)	112 (100.0)	207 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.082

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.4 (95.1, 99.7)
6 months	100.0 (100.0, 100.0)	97.4 (95.1, 99.7)
9 months	100.0 (100.0, 100.0)	97.4 (95.1, 99.7)
12 months	100.0 (100.0, 100.0)	97.4 (95.1, 99.7)
18 months	NE (NE, NE)	97.4 (95.1, 99.7)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	25 (22.3)	80 (37.7)
Number of Subjects Censored, n (%)	87 (77.7)	132 (62.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.02, NE)	0.89 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	NE (9.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.593 (0.232)
95% CI		(1.011, 2.509)
Log-rank p-value		0.039

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.1 (67.7, 84.4)	64.5 (57.9, 71.0)
6 months	76.1 (67.7, 84.4)	59.2 (51.7, 66.8)
9 months	76.1 (67.7, 84.4)	59.2 (51.7, 66.8)
12 months	76.1 (67.7, 84.4)	55.5 (45.6, 65.5)
18 months	NE (NE, NE)	55.5 (45.6, 65.5)
Median Follow-up Time (months)	2.43	2.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	5 (4.5)	36 (17.0)
Number of Subjects Censored, n (%)	107 (95.5)	176 (83.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.684 (0.480)
95% CI		(1.438, 9.434)
Log-rank p-value		0.004

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (91.6, 99.3)	82.8 (77.7, 87.9)
6 months	95.5 (91.6, 99.3)	82.8 (77.7, 87.9)
9 months	95.5 (91.6, 99.3)	82.8 (77.7, 87.9)
12 months	95.5 (91.6, 99.3)	82.8 (77.7, 87.9)
18 months	NE (NE, NE)	82.8 (77.7, 87.9)
Median Follow-up Time (months)	2.79	3.37

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	10 (8.9)	22 (10.4)
Number of Subjects Censored, n (%)	102 (91.1)	190 (89.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.915 (0.389)
95% CI		(0.426, 1.962)
Log-rank p-value		0.874

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.6 (85.0, 96.2)	91.3 (87.4, 95.1)
6 months	90.6 (85.0, 96.2)	88.3 (83.3, 93.4)
9 months	90.6 (85.0, 96.2)	86.7 (80.9, 92.6)
12 months	90.6 (85.0, 96.2)	86.7 (80.9, 92.6)
18 months	NE (NE, NE)	86.7 (80.9, 92.6)
Median Follow-up Time (months)	2.79	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	8 (7.1)	13 (6.1)
Number of Subjects Censored, n (%)	104 (92.9)	199 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.804 (0.451)
95% CI		(0.332, 1.946)
Log-rank p-value		0.597

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.4 (87.3, 97.5)	93.8 (90.5, 97.1)
6 months	92.4 (87.3, 97.5)	93.8 (90.5, 97.1)
9 months	92.4 (87.3, 97.5)	93.8 (90.5, 97.1)
12 months	92.4 (87.3, 97.5)	93.8 (90.5, 97.1)
18 months	NE (NE, NE)	93.8 (90.5, 97.1)
Median Follow-up Time (months)	2.68	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	1 (0.9)	7 (3.3)
Number of Subjects Censored, n (%)	111 (99.1)	205 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.615 (1.072)
95% CI		(0.442, 29.553)
Log-rank p-value		0.206

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.4, 100.0)	96.5 (93.9, 99.1)
6 months	99.1 (97.4, 100.0)	96.5 (93.9, 99.1)
9 months	99.1 (97.4, 100.0)	96.5 (93.9, 99.1)
12 months	99.1 (97.4, 100.0)	96.5 (93.9, 99.1)
18 months	NE (NE, NE)	96.5 (93.9, 99.1)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	0	1 (0.5)
Number of Subjects Censored, n (%)	112 (100.0)	211 (99.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.490

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.5 (98.6, 100.0)
6 months	100.0 (100.0, 100.0)	99.5 (98.6, 100.0)
9 months	100.0 (100.0, 100.0)	99.5 (98.6, 100.0)
12 months	100.0 (100.0, 100.0)	99.5 (98.6, 100.0)
18 months	NE (NE, NE)	99.5 (98.6, 100.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Vascular disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	19 (17.0)	77 (36.3)
Number of Subjects Censored, n (%)	93 (83.0)	135 (63.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.87, NE)	0.95 (0.69, 2.07)
Median (95% CI)	NE (NE, NE)	NE (7.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.172 (0.259)
95% CI		(1.307, 3.610)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Vascular disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.9 (75.7, 90.1)	65.8 (59.3, 72.4)
6 months	76.0 (61.5, 90.6)	59.5 (51.4, 67.6)
9 months	NE (NE, NE)	53.5 (42.9, 64.2)
12 months	NE (NE, NE)	53.5 (42.9, 64.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	2.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	11 (9.8)	73 (34.4)
Number of Subjects Censored, n (%)	101 (90.2)	139 (65.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.12 (0.69, 2.53)
Median (95% CI)	NE (NE, NE)	NE (7.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.592 (0.326)
95% CI		(1.895, 6.806)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.7 (83.9, 95.5)	67.7 (61.2, 74.2)
6 months	89.7 (83.9, 95.5)	63.1 (55.6, 70.6)
9 months	NE (NE, NE)	54.6 (43.6, 65.7)
12 months	NE (NE, NE)	54.6 (43.6, 65.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	24 (21.4)	70 (33.0)
Number of Subjects Censored, n (%)	88 (78.6)	142 (67.0)
Time to first TEAE (months)		
25% percentile (95% CI)	3.71 (1.81, NE)	1.64 (0.76, 3.09)
Median (95% CI)	5.59 (5.59, NE)	NE (7.66, NE)
75% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.359 (0.242)
95% CI		(0.846, 2.184)
Log-rank p-value		0.203

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.9 (69.4, 86.4)	69.3 (62.9, 75.6)
6 months	47.6 (8.3, 86.9)	64.6 (57.1, 72.1)
9 months	NE (NE, NE)	56.1 (44.8, 67.4)
12 months	NE (NE, NE)	56.1 (44.8, 67.4)
18 months	NE (NE, NE)	56.1 (44.8, 67.4)
Median Follow-up Time (months)	2.38	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	9 (8.0)	18 (8.5)
Number of Subjects Censored, n (%)	103 (92.0)	194 (91.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.878 (0.415)
95% CI		(0.390, 1.981)
Log-rank p-value		0.788

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.6 (86.4, 96.9)	92.0 (88.3, 95.8)
6 months	91.6 (86.4, 96.9)	90.0 (85.3, 94.7)
9 months	91.6 (86.4, 96.9)	90.0 (85.3, 94.7)
12 months	91.6 (86.4, 96.9)	90.0 (85.3, 94.7)
18 months	NE (NE, NE)	90.0 (85.3, 94.7)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	5 (4.5)	20 (9.4)
Number of Subjects Censored, n (%)	107 (95.5)	192 (90.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.919 (0.508)
95% CI		(0.709, 5.196)
Log-rank p-value		0.201

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.2 (92.6, 99.9)	91.3 (87.5, 95.2)
6 months	80.2 (51.3, 100.0)	90.4 (86.1, 94.6)
9 months	NE (NE, NE)	88.0 (81.8, 94.2)
12 months	NE (NE, NE)	88.0 (81.8, 94.2)
18 months	NE (NE, NE)	88.0 (81.8, 94.2)
Median Follow-up Time (months)	2.79	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	2 (1.8)	16 (7.5)
Number of Subjects Censored, n (%)	110 (98.2)	196 (92.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.187 (0.755)
95% CI		(0.725, 14.000)
Log-rank p-value		0.104

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.7, 100.0)	92.6 (88.9, 96.2)
6 months	93.1 (81.8, 100.0)	91.1 (86.6, 95.7)
9 months	93.1 (81.8, 100.0)	91.1 (86.6, 95.7)
12 months	93.1 (81.8, 100.0)	91.1 (86.6, 95.7)
18 months	NE (NE, NE)	91.1 (86.6, 95.7)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	1 (0.9)	5 (2.4)
Number of Subjects Censored, n (%)	111 (99.1)	207 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.574 (1.099)
95% CI		(0.299, 22.185)
Log-rank p-value		0.395

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.3, 100.0)	97.4 (95.2, 99.7)
6 months	99.1 (97.3, 100.0)	97.4 (95.2, 99.7)
9 months	99.1 (97.3, 100.0)	97.4 (95.2, 99.7)
12 months	99.1 (97.3, 100.0)	97.4 (95.2, 99.7)
18 months	NE (NE, NE)	97.4 (95.2, 99.7)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	2 (1.8)	6 (2.8)
Number of Subjects Censored, n (%)	110 (98.2)	206 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.249 (0.829)
95% CI		(0.246, 6.344)
Log-rank p-value		0.771

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (95.6, 100.0)	97.6 (95.5, 99.7)
6 months	98.2 (95.6, 100.0)	97.6 (95.5, 99.7)
9 months	98.2 (95.6, 100.0)	94.1 (87.1, 100.0)
12 months	98.2 (95.6, 100.0)	94.1 (87.1, 100.0)
18 months	NE (NE, NE)	94.1 (87.1, 100.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	0	1 (0.5)
Number of Subjects Censored, n (%)	112 (100.0)	211 (99.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.525

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.5 (98.5, 100.0)
6 months	100.0 (100.0, 100.0)	99.5 (98.5, 100.0)
9 months	100.0 (100.0, 100.0)	99.5 (98.5, 100.0)
12 months	100.0 (100.0, 100.0)	99.5 (98.5, 100.0)
18 months	NE (NE, NE)	99.5 (98.5, 100.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	12 (10.7)	62 (29.2)
Number of Subjects Censored, n (%)	100 (89.3)	150 (70.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	2.04 (0.99, 4.86)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.963 (0.320)
95% CI		(1.581, 5.551)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (83.0, 94.8)	72.2 (66.0, 78.4)
6 months	88.9 (83.0, 94.8)	65.8 (58.0, 73.7)
9 months	88.9 (83.0, 94.8)	65.8 (58.0, 73.7)
12 months	88.9 (83.0, 94.8)	65.8 (58.0, 73.7)
18 months	NE (NE, NE)	65.8 (58.0, 73.7)
Median Follow-up Time (months)	2.68	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	1 (0.9)	36 (17.0)
Number of Subjects Censored, n (%)	111 (99.1)	176 (83.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.86, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		18.939 (1.016)
95% CI		(2.586, 138.719)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.4, 100.0)	84.8 (79.9, 89.8)
6 months	99.1 (97.4, 100.0)	78.4 (71.0, 85.7)
9 months	99.1 (97.4, 100.0)	78.4 (71.0, 85.7)
12 months	99.1 (97.4, 100.0)	78.4 (71.0, 85.7)
18 months	NE (NE, NE)	78.4 (71.0, 85.7)
Median Follow-up Time (months)	2.79	3.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	3 (2.7)	5 (2.4)
Number of Subjects Censored, n (%)	109 (97.3)	207 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.940 (0.735)
95% CI		(0.223, 3.970)
Log-rank p-value		0.913

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (94.3, 100.0)	97.6 (95.6, 99.7)
6 months	97.3 (94.3, 100.0)	97.6 (95.6, 99.7)
9 months	97.3 (94.3, 100.0)	97.6 (95.6, 99.7)
12 months	97.3 (94.3, 100.0)	97.6 (95.6, 99.7)
18 months	NE (NE, NE)	97.6 (95.6, 99.7)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	0	6 (2.8)
Number of Subjects Censored, n (%)	112 (100.0)	206 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.104

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.0 (94.6, 99.4)
6 months	100.0 (100.0, 100.0)	97.0 (94.6, 99.4)
9 months	100.0 (100.0, 100.0)	97.0 (94.6, 99.4)
12 months	100.0 (100.0, 100.0)	97.0 (94.6, 99.4)
18 months	NE (NE, NE)	97.0 (94.6, 99.4)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Nervous system disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	18 (16.1)	55 (25.9)
Number of Subjects Censored, n (%)	94 (83.9)	157 (74.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.50, NE)	2.99 (1.58, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.558 (0.276)
95% CI		(0.908, 2.674)
Log-rank p-value		0.174

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Nervous system disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.9 (74.2, 89.7)	74.8 (68.8, 80.9)
6 months	81.9 (74.2, 89.7)	70.5 (63.3, 77.6)
9 months	81.9 (74.2, 89.7)	70.5 (63.3, 77.6)
12 months	81.9 (74.2, 89.7)	70.5 (63.3, 77.6)
18 months	NE (NE, NE)	70.5 (63.3, 77.6)
Median Follow-up Time (months)	2.56	3.07

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	3 (2.7)	18 (8.5)
Number of Subjects Censored, n (%)	109 (97.3)	194 (91.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.008 (0.626)
95% CI		(0.881, 10.268)
Log-rank p-value		0.066

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.0 (93.8, 100.0)	91.8 (88.1, 95.6)
6 months	97.0 (93.8, 100.0)	90.7 (86.5, 95.0)
9 months	97.0 (93.8, 100.0)	90.7 (86.5, 95.0)
12 months	97.0 (93.8, 100.0)	90.7 (86.5, 95.0)
18 months	NE (NE, NE)	90.7 (86.5, 95.0)
Median Follow-up Time (months)	2.79	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	5 (4.5)	6 (2.8)
Number of Subjects Censored, n (%)	107 (95.5)	206 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.579 (0.612)
95% CI		(0.175, 1.920)
Log-rank p-value		0.359

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (91.5, 99.3)	96.9 (94.5, 99.4)
6 months	95.4 (91.5, 99.3)	96.9 (94.5, 99.4)
9 months	95.4 (91.5, 99.3)	96.9 (94.5, 99.4)
12 months	95.4 (91.5, 99.3)	96.9 (94.5, 99.4)
18 months	NE (NE, NE)	96.9 (94.5, 99.4)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	3 (2.7)	6 (2.8)
Number of Subjects Censored, n (%)	109 (97.3)	206 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.819 (0.715)
95% CI		(0.202, 3.325)
Log-rank p-value		0.840

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.0 (93.7, 100.0)	97.0 (94.6, 99.4)
6 months	97.0 (93.7, 100.0)	97.0 (94.6, 99.4)
9 months	97.0 (93.7, 100.0)	97.0 (94.6, 99.4)
12 months	97.0 (93.7, 100.0)	97.0 (94.6, 99.4)
18 months	NE (NE, NE)	97.0 (94.6, 99.4)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	19 (17.0)	57 (26.9)
Number of Subjects Censored, n (%)	93 (83.0)	155 (73.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.87, NE)	2.83 (2.10, 6.47)
Median (95% CI)	NE (NE, NE)	NE (11.96, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.394 (0.269)
95% CI		(0.822, 2.363)
Log-rank p-value		0.327

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.6 (72.5, 88.7)	74.6 (68.4, 80.7)
6 months	80.6 (72.5, 88.7)	68.2 (60.3, 76.1)
9 months	80.6 (72.5, 88.7)	66.3 (57.7, 74.8)
12 months	80.6 (72.5, 88.7)	53.0 (28.8, 77.2)
18 months	NE (NE, NE)	53.0 (28.8, 77.2)
Median Follow-up Time (months)	2.38	3.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	7 (6.3)	39 (18.4)
Number of Subjects Censored, n (%)	105 (93.8)	173 (81.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.65, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.588 (0.413)
95% CI		(1.152, 5.813)
Log-rank p-value		0.019

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.1 (88.1, 98.1)	81.6 (76.1, 87.1)
6 months	93.1 (88.1, 98.1)	79.6 (73.6, 85.6)
9 months	93.1 (88.1, 98.1)	75.8 (66.6, 85.0)
12 months	93.1 (88.1, 98.1)	75.8 (66.6, 85.0)
18 months	NE (NE, NE)	75.8 (66.6, 85.0)
Median Follow-up Time (months)	2.68	3.37

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	4 (3.6)	6 (2.8)
Number of Subjects Censored, n (%)	108 (96.4)	206 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.905 (0.659)
95% CI		(0.249, 3.291)
Log-rank p-value		0.819

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.2 (92.5, 99.9)	97.1 (94.9, 99.4)
6 months	96.2 (92.5, 99.9)	97.1 (94.9, 99.4)
9 months	96.2 (92.5, 99.9)	97.1 (94.9, 99.4)
12 months	96.2 (92.5, 99.9)	97.1 (94.9, 99.4)
18 months	NE (NE, NE)	97.1 (94.9, 99.4)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Infections and infestations**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	13 (11.6)	37 (17.5)
Number of Subjects Censored, n (%)	99 (88.4)	175 (82.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.15, NE)	6.93 (5.72, NE)
Median (95% CI)	NE (NE, NE)	17.48 (17.48, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.48, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.069 (0.336)
95% CI		(0.553, 2.066)
Log-rank p-value		0.647

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Infections and infestations**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (82.5, 95.2)	87.1 (82.5, 91.8)
6 months	77.6 (61.4, 93.7)	79.4 (72.2, 86.6)
9 months	77.6 (61.4, 93.7)	73.7 (64.5, 82.8)
12 months	77.6 (61.4, 93.7)	73.7 (64.5, 82.8)
18 months	NE (NE, NE)	49.1 (9.3, 88.9)
Median Follow-up Time (months)	2.68	3.56

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	4 (3.6)	11 (5.2)
Number of Subjects Censored, n (%)	108 (96.4)	201 (94.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.870 (0.613)
95% CI		(0.261, 2.895)
Log-rank p-value		0.852

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (95.6, 100.0)	96.5 (94.0, 99.1)
6 months	88.8 (76.1, 100.0)	95.6 (92.4, 98.7)
9 months	88.8 (76.1, 100.0)	89.8 (82.9, 96.8)
12 months	88.8 (76.1, 100.0)	89.8 (82.9, 96.8)
18 months	NE (NE, NE)	89.8 (82.9, 96.8)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	5 (4.5)	2 (0.9)
Number of Subjects Censored, n (%)	107 (95.5)	210 (99.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.170 (0.921)
95% CI		(0.028, 1.035)
Log-rank p-value		0.051

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (90.4, 99.3)	99.5 (98.6, 100.0)
6 months	94.9 (90.4, 99.3)	98.4 (96.1, 100.0)
9 months	94.9 (90.4, 99.3)	98.4 (96.1, 100.0)
12 months	94.9 (90.4, 99.3)	98.4 (96.1, 100.0)
18 months	NE (NE, NE)	98.4 (96.1, 100.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	0	5 (2.4)
Number of Subjects Censored, n (%)	112 (100.0)	207 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.117

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.4 (95.2, 99.7)
6 months	100.0 (100.0, 100.0)	97.4 (95.2, 99.7)
9 months	100.0 (100.0, 100.0)	97.4 (95.2, 99.7)
12 months	100.0 (100.0, 100.0)	97.4 (95.2, 99.7)
18 months	NE (NE, NE)	97.4 (95.2, 99.7)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	22 (19.6)	34 (16.0)
Number of Subjects Censored, n (%)	90 (80.4)	178 (84.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.84, NE)	NE (6.41, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.673 (0.280)
95% CI		(0.389, 1.163)
Log-rank p-value		0.175

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.5 (69.0, 86.1)	84.6 (79.6, 89.6)
6 months	77.5 (69.0, 86.1)	82.8 (77.4, 88.3)
9 months	77.5 (69.0, 86.1)	81.0 (74.6, 87.4)
12 months	77.5 (69.0, 86.1)	81.0 (74.6, 87.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.38	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	17 (15.2)	19 (9.0)
Number of Subjects Censored, n (%)	95 (84.8)	193 (91.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.79, NE)	17.74 (17.74, NE)
Median (95% CI)	NE (NE, NE)	17.74 (17.74, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.74, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.447 (0.349)
95% CI		(0.226, 0.886)
Log-rank p-value		0.017

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.0 (74.0, 90.1)	92.4 (88.6, 96.1)
6 months	82.0 (74.0, 90.1)	90.6 (86.3, 95.0)
9 months	82.0 (74.0, 90.1)	89.0 (83.6, 94.3)
12 months	82.0 (74.0, 90.1)	89.0 (83.6, 94.3)
18 months	NE (NE, NE)	44.5 (0.0, 100.0)
Median Follow-up Time (months)	2.46	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	2 (1.8)	18 (8.5)
Number of Subjects Censored, n (%)	110 (98.2)	194 (91.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.1, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.763 (0.751)
95% CI		(1.093, 20.759)
Log-rank p-value		0.021

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (95.4, 100.0)	91.2 (87.2, 95.1)
6 months	98.1 (95.4, 100.0)	91.2 (87.2, 95.1)
9 months	98.1 (95.4, 100.0)	91.2 (87.2, 95.1)
12 months	98.1 (95.4, 100.0)	91.2 (87.2, 95.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Endocrine disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	1 (0.9)	49 (23.1)
Number of Subjects Censored, n (%)	111 (99.1)	163 (76.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.37 (2.76, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		21.751 (1.012)
95% CI		(2.991, 158.160)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Endocrine disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.3, 100.0)	80.6 (75.0, 86.1)
6 months	99.1 (97.3, 100.0)	67.8 (59.0, 76.6)
9 months	99.1 (97.3, 100.0)	67.8 (59.0, 76.6)
12 months	99.1 (97.3, 100.0)	67.8 (59.0, 76.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	1 (0.9)	47 (22.2)
Number of Subjects Censored, n (%)	111 (99.1)	165 (77.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.63 (3.42, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		20.606 (1.013)
95% CI		(2.830, 150.026)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.3, 100.0)	81.5 (76.0, 87.0)
6 months	99.1 (97.3, 100.0)	68.8 (60.1, 77.5)
9 months	99.1 (97.3, 100.0)	68.8 (60.1, 77.5)
12 months	99.1 (97.3, 100.0)	68.8 (60.1, 77.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.37

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Psychiatric disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	7 (6.3)	28 (13.2)
Number of Subjects Censored, n (%)	105 (93.8)	184 (86.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.72, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.686 (0.437)
95% CI		(0.717, 3.968)
Log-rank p-value		0.298

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Psychiatric disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.2 (89.6, 98.7)	90.1 (85.9, 94.2)
6 months	90.6 (82.3, 98.8)	81.8 (75.0, 88.6)
9 months	90.6 (82.3, 98.8)	81.8 (75.0, 88.6)
12 months	90.6 (82.3, 98.8)	81.8 (75.0, 88.6)
18 months	NE (NE, NE)	81.8 (75.0, 88.6)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	5 (4.5)	9 (4.2)
Number of Subjects Censored, n (%)	107 (95.5)	203 (95.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.850 (0.586)
95% CI		(0.270, 2.683)
Log-rank p-value		0.668

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (90.9, 99.3)	96.8 (94.3, 99.4)
6 months	95.1 (90.9, 99.3)	94.1 (90.1, 98.1)
9 months	95.1 (90.9, 99.3)	94.1 (90.1, 98.1)
12 months	95.1 (90.9, 99.3)	94.1 (90.1, 98.1)
18 months	NE (NE, NE)	94.1 (90.1, 98.1)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	2 (1.8)	5 (2.4)
Number of Subjects Censored, n (%)	110 (98.2)	207 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.896 (0.864)
95% CI		(0.165, 4.871)
Log-rank p-value		0.793

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (96.9, 100.0)	98.1 (96.2, 99.9)
6 months	95.2 (87.6, 100.0)	96.7 (93.5, 99.9)
9 months	95.2 (87.6, 100.0)	96.7 (93.5, 99.9)
12 months	95.2 (87.6, 100.0)	96.7 (93.5, 99.9)
18 months	NE (NE, NE)	96.7 (93.5, 99.9)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	0	8 (3.8)
Number of Subjects Censored, n (%)	112 (100.0)	204 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.115

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.0 (94.6, 99.4)
6 months	100.0 (100.0, 100.0)	94.8 (90.9, 98.7)
9 months	100.0 (100.0, 100.0)	94.8 (90.9, 98.7)
12 months	100.0 (100.0, 100.0)	94.8 (90.9, 98.7)
18 months	NE (NE, NE)	94.8 (90.9, 98.7)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	14 (12.5)	21 (9.9)
Number of Subjects Censored, n (%)	98 (87.5)	191 (90.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.15, NE)	NE (9.66, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.597 (0.356)
95% CI		(0.298, 1.199)
Log-rank p-value		0.214

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.8 (81.5, 94.0)	91.3 (87.4, 95.3)
6 months	84.3 (75.3, 93.3)	88.2 (83.0, 93.4)
9 months	84.3 (75.3, 93.3)	88.2 (83.0, 93.4)
12 months	84.3 (75.3, 93.3)	83.8 (74.0, 93.6)
18 months	NE (NE, NE)	83.8 (74.0, 93.6)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	2 (1.8)	8 (3.8)
Number of Subjects Censored, n (%)	110 (98.2)	204 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.66, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.385 (0.807)
95% CI		(0.285, 6.735)
Log-rank p-value		0.740

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (95.3, 100.0)	96.8 (94.2, 99.3)
6 months	98.0 (95.3, 100.0)	95.9 (92.7, 99.0)
9 months	98.0 (95.3, 100.0)	95.9 (92.7, 99.0)
12 months	98.0 (95.3, 100.0)	91.1 (81.4, 100.0)
18 months	NE (NE, NE)	91.1 (81.4, 100.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Number of Subjects with Events, n (%)	2 (1.8)	4 (1.9)
Number of Subjects Censored, n (%)	110 (98.2)	208 (98.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.802 (0.894)
95% CI		(0.139, 4.626)
Log-rank p-value		0.791

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3B
Summary of Time to Onset of TEAE by SOC/PT by Age
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
>=65 years

Statistics	Placebo + BSC N=112	Fruquintinib + BSC N=212
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (95.7, 100.0)	98.5 (96.9, 100.0)
6 months	98.2 (95.7, 100.0)	97.1 (93.8, 100.0)
9 months	98.2 (95.7, 100.0)	97.1 (93.8, 100.0)
12 months	98.2 (95.7, 100.0)	97.1 (93.8, 100.0)
18 months	NE (NE, NE)	97.1 (93.8, 100.0)
Median Follow-up Time (months)	2.79	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	80 (57.1)	167 (69.3)
Number of Subjects Censored, n (%)	60 (42.9)	74 (30.7)
Time to first TEAE (months)		
25% percentile (95% CI)	0.56 (0.30, 0.69)	0.39 (0.26, 0.66)
Median (95% CI)	1.84 (1.22, 3.19)	1.12 (0.85, 1.84)
75% percentile (95% CI)	NE (4.70, NE)	6.93 (4.37, NE)
Min, Max	0.0, 13.0*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.162 (0.138)
95% CI		(0.886, 1.525)
Log-rank p-value		0.356

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	43.2 (34.8, 51.7)	38.1 (31.9, 44.3)
6 months	28.4 (10.5, 46.2)	26.7 (20.0, 33.4)
9 months	28.4 (10.5, 46.2)	18.2 (9.7, 26.7)
12 months	28.4 (10.5, 46.2)	18.2 (9.7, 26.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.45	1.12

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	31 (22.1)	81 (33.6)
Number of Subjects Censored, n (%)	109 (77.9)	160 (66.4)
Time to first TEAE (months)		
25% percentile (95% CI)	4.70 (1.35, NE)	1.05 (0.69, 2.60)
Median (95% CI)	NE (NE, NE)	NE (8.41, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.440 (0.213)
95% CI		(0.948, 2.186)
Log-rank p-value		0.108

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.1 (69.8, 84.4)	68.7 (62.8, 74.7)
6 months	69.4 (53.6, 85.2)	65.5 (59.2, 71.8)
9 months	69.4 (53.6, 85.2)	60.2 (50.5, 69.8)
12 months	69.4 (53.6, 85.2)	60.2 (50.5, 69.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.73	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	23 (16.4)	52 (21.6)
Number of Subjects Censored, n (%)	117 (83.6)	189 (78.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.60, NE)	7.29 (2.73, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.197 (0.254)
95% CI		(0.728, 1.970)
Log-rank p-value		0.497

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.1 (75.4, 88.9)	79.3 (74.1, 84.6)
6 months	82.1 (75.4, 88.9)	77.9 (72.4, 83.4)
9 months	82.1 (75.4, 88.9)	73.1 (64.8, 81.4)
12 months	82.1 (75.4, 88.9)	73.1 (64.8, 81.4)
18 months	NE (NE, NE)	73.1 (64.8, 81.4)
Median Follow-up Time (months)	2.46	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	15 (10.7)	29 (12.0)
Number of Subjects Censored, n (%)	125 (89.3)	212 (88.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.70, NE)	NE (11.53, NE)
Median (95% CI)	NE (4.70, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.817 (0.333)
95% CI		(0.426, 1.567)
Log-rank p-value		0.534

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.6 (82.9, 94.4)	90.5 (86.7, 94.3)
6 months	77.5 (56.6, 98.5)	87.4 (82.6, 92.1)
9 months	77.5 (56.6, 98.5)	84.4 (78.3, 90.5)
12 months	77.5 (56.6, 98.5)	76.7 (61.4, 92.1)
18 months	NE (NE, NE)	76.7 (61.4, 92.1)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	3 (2.1)	28 (11.6)
Number of Subjects Censored, n (%)	137 (97.9)	213 (88.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
Median (95% CI)	NE (NE, NE)	NE (13.24, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.24, NE)
Min, Max	0.2*, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.013 (0.611)
95% CI		(1.514, 16.597)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (94.9, 100.0)	89.5 (85.6, 93.4)
6 months	97.6 (94.9, 100.0)	88.8 (84.7, 92.9)
9 months	97.6 (94.9, 100.0)	86.8 (81.2, 92.4)
12 months	97.6 (94.9, 100.0)	86.8 (81.2, 92.4)
18 months	NE (NE, NE)	57.8 (11.4, 100.0)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	19 (13.6)	15 (6.2)
Number of Subjects Censored, n (%)	121 (86.4)	226 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.19, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.323 (0.358)
95% CI		(0.160, 0.651)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.5 (80.4, 92.5)	95.7 (93.1, 98.3)
6 months	79.8 (69.1, 90.5)	92.0 (87.9, 96.1)
9 months	79.8 (69.1, 90.5)	92.0 (87.9, 96.1)
12 months	79.8 (69.1, 90.5)	92.0 (87.9, 96.1)
18 months	NE (NE, NE)	92.0 (87.9, 96.1)
Median Follow-up Time (months)	2.83	4.11

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	10 (7.1)	9 (3.7)
Number of Subjects Censored, n (%)	130 (92.9)	232 (96.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.99, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.366 (0.485)
95% CI		(0.141, 0.947)
Log-rank p-value		0.026

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.2 (87.4, 96.9)	97.0 (94.8, 99.2)
6 months	92.2 (87.4, 96.9)	97.0 (94.8, 99.2)
9 months	92.2 (87.4, 96.9)	93.0 (84.9, 100.0)
12 months	92.2 (87.4, 96.9)	87.8 (75.4, 100.0)
18 months	NE (NE, NE)	87.8 (75.4, 100.0)
Median Follow-up Time (months)	2.81	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	3 (2.1)	8 (3.3)
Number of Subjects Censored, n (%)	137 (97.9)	233 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.82, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.927 (0.706)
95% CI		(0.233, 3.698)
Log-rank p-value		0.903

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (94.8, 100.0)	98.2 (96.5, 100.0)
6 months	97.5 (94.8, 100.0)	96.1 (93.1, 99.0)
9 months	97.5 (94.8, 100.0)	96.1 (93.1, 99.0)
12 months	97.5 (94.8, 100.0)	91.0 (81.0, 100.0)
18 months	NE (NE, NE)	91.0 (81.0, 100.0)
Median Follow-up Time (months)	2.83	4.07

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	1 (0.7)	4 (1.7)
Number of Subjects Censored, n (%)	139 (99.3)	237 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.439 (1.147)
95% CI		(0.152, 13.612)
Log-rank p-value		0.818

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	98.6 (96.9, 100.0)
6 months	99.3 (97.8, 100.0)	97.7 (95.4, 100.0)
9 months	99.3 (97.8, 100.0)	97.7 (95.4, 100.0)
12 months	99.3 (97.8, 100.0)	97.7 (95.4, 100.0)
18 months	NE (NE, NE)	97.7 (95.4, 100.0)
Median Follow-up Time (months)	2.83	4.11

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	1 (0.7)	7 (2.9)
Number of Subjects Censored, n (%)	139 (99.3)	234 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.380 (1.088)
95% CI		(0.400, 28.536)
Log-rank p-value		0.225

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	97.9 (96.1, 99.7)
6 months	99.3 (97.8, 100.0)	96.4 (93.0, 99.8)
9 months	99.3 (97.8, 100.0)	92.9 (85.3, 100.0)
12 months	99.3 (97.8, 100.0)	92.9 (85.3, 100.0)
18 months	NE (NE, NE)	92.9 (85.3, 100.0)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	78 (55.7)	164 (68.0)
Number of Subjects Censored, n (%)	62 (44.3)	77 (32.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.49 (0.26, 0.69)	0.56 (0.39, 0.69)
Median (95% CI)	1.71 (1.38, 2.92)	1.35 (0.92, 1.84)
75% percentile (95% CI)	5.59 (3.35, NE)	6.70 (4.90, NE)
Min, Max	0.0, 5.6	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.078 (0.141)
95% CI		(0.817, 1.422)
Log-rank p-value		0.643

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	39.8 (29.6, 49.9)	36.4 (30.1, 42.7)
6 months	0.0 (NE, NE)	27.4 (20.4, 34.4)
9 months	0.0 (NE, NE)	16.4 (7.6, 25.1)
12 months	0.0 (NE, NE)	16.4 (7.6, 25.1)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.40	1.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	18 (12.9)	60 (24.9)
Number of Subjects Censored, n (%)	122 (87.1)	181 (75.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.39 (2.37, 6.47)
Median (95% CI)	NE (NE, NE)	NE (10.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.582 (0.274)
95% CI		(0.924, 2.708)
Log-rank p-value		0.103

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.6 (80.9, 92.4)	78.9 (73.6, 84.2)
6 months	86.6 (80.9, 92.4)	70.5 (62.9, 78.0)
9 months	86.6 (80.9, 92.4)	67.3 (58.9, 75.7)
12 months	86.6 (80.9, 92.4)	57.7 (38.8, 76.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.61	2.89

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	21 (15.0)	41 (17.0)
Number of Subjects Censored, n (%)	119 (85.0)	200 (83.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.03, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.847 (0.277)
95% CI		(0.492, 1.458)
Log-rank p-value		0.531

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.4 (78.2, 90.6)	85.1 (80.4, 89.7)
6 months	84.4 (78.2, 90.6)	79.3 (72.9, 85.7)
9 months	84.4 (78.2, 90.6)	79.3 (72.9, 85.7)
12 months	84.4 (78.2, 90.6)	75.2 (65.1, 85.2)
18 months	NE (NE, NE)	75.2 (65.1, 85.2)
Median Follow-up Time (months)	2.73	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	21 (15.0)	43 (17.8)
Number of Subjects Censored, n (%)	119 (85.0)	198 (82.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.92, NE)	9.23 (4.21, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.934 (0.274)
95% CI		(0.546, 1.597)
Log-rank p-value		0.959

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.0 (75.3, 90.6)	83.7 (78.7, 88.6)
6 months	76.6 (62.6, 90.5)	80.8 (75.3, 86.3)
9 months	76.6 (62.6, 90.5)	77.8 (71.1, 84.5)
12 months	76.6 (62.6, 90.5)	73.7 (63.6, 83.8)
18 months	NE (NE, NE)	73.7 (63.6, 83.8)
Median Follow-up Time (months)	2.79	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	12 (8.6)	43 (17.8)
Number of Subjects Censored, n (%)	128 (91.4)	198 (82.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	7.10 (4.21, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.485 (0.334)
95% CI		(0.772, 2.856)
Log-rank p-value		0.296

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.8 (83.1, 96.5)	84.6 (79.7, 89.4)
6 months	86.9 (78.3, 95.5)	80.8 (75.2, 86.5)
9 months	86.9 (78.3, 95.5)	74.3 (65.5, 83.1)
12 months	86.9 (78.3, 95.5)	70.2 (58.7, 81.6)
18 months	NE (NE, NE)	70.2 (58.7, 81.6)
Median Follow-up Time (months)	2.79	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	12 (8.6)	25 (10.4)
Number of Subjects Censored, n (%)	128 (91.4)	216 (89.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.52, NE)	18.04 (9.20, NE)
Median (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.853 (0.368)
95% CI		(0.415, 1.754)
Log-rank p-value		0.665

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.7 (87.0, 96.4)	91.7 (88.1, 95.3)
6 months	87.6 (78.4, 96.7)	88.8 (83.9, 93.6)
9 months	87.6 (78.4, 96.7)	87.3 (81.7, 92.9)
12 months	87.6 (78.4, 96.7)	83.2 (73.6, 92.7)
18 months	NE (NE, NE)	83.2 (73.6, 92.7)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	5 (3.6)	35 (14.5)
Number of Subjects Censored, n (%)	135 (96.4)	206 (85.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.898 (0.479)
95% CI		(1.523, 9.977)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.1 (92.7, 99.5)	85.6 (81.1, 90.1)
6 months	96.1 (92.7, 99.5)	84.7 (79.9, 89.5)
9 months	96.1 (92.7, 99.5)	84.7 (79.9, 89.5)
12 months	96.1 (92.7, 99.5)	84.7 (79.9, 89.5)
18 months	NE (NE, NE)	84.7 (79.9, 89.5)
Median Follow-up Time (months)	2.79	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	8 (5.7)	14 (5.8)
Number of Subjects Censored, n (%)	132 (94.3)	227 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.3, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.761 (0.462)
95% CI		(0.307, 1.882)
Log-rank p-value		0.539

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.7 (90.8, 98.5)	95.3 (92.5, 98.0)
6 months	78.9 (50.5, 100.0)	93.8 (90.4, 97.2)
9 months	NE (NE, NE)	91.1 (85.0, 97.2)
12 months	NE (NE, NE)	91.1 (85.0, 97.2)
18 months	NE (NE, NE)	91.1 (85.0, 97.2)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	3 (2.1)	12 (5.0)
Number of Subjects Censored, n (%)	137 (97.9)	229 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.982 (0.656)
95% CI		(0.548, 7.169)
Log-rank p-value		0.254

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (94.9, 100.0)	95.8 (93.3, 98.4)
6 months	97.6 (94.9, 100.0)	94.9 (91.9, 98.0)
9 months	97.6 (94.9, 100.0)	92.4 (86.6, 98.1)
12 months	97.6 (94.9, 100.0)	92.4 (86.6, 98.1)
18 months	NE (NE, NE)	92.4 (86.6, 98.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	3 (2.1)	6 (2.5)
Number of Subjects Censored, n (%)	137 (97.9)	235 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.895 (0.714)
95% CI		(0.221, 3.630)
Log-rank p-value		0.974

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (94.5, 100.0)	97.3 (95.1, 99.5)
6 months	97.4 (94.5, 100.0)	97.3 (95.1, 99.5)
9 months	97.4 (94.5, 100.0)	97.3 (95.1, 99.5)
12 months	97.4 (94.5, 100.0)	97.3 (95.1, 99.5)
18 months	NE (NE, NE)	97.3 (95.1, 99.5)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	6 (4.3)	0
Number of Subjects Censored, n (%)	134 (95.7)	241 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.3 (91.6, 99.0)	100.0 (100.0, 100.0)
6 months	95.3 (91.6, 99.0)	100.0 (100.0, 100.0)
9 months	95.3 (91.6, 99.0)	100.0 (100.0, 100.0)
12 months	95.3 (91.6, 99.0)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	4.11

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	0	6 (2.5)
Number of Subjects Censored, n (%)	140 (100.0)	235 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.074

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.3 (95.2, 99.4)
6 months	100.0 (100.0, 100.0)	97.3 (95.2, 99.4)
9 months	100.0 (100.0, 100.0)	97.3 (95.2, 99.4)
12 months	100.0 (100.0, 100.0)	97.3 (95.2, 99.4)
18 months	NE (NE, NE)	97.3 (95.2, 99.4)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	37 (26.4)	106 (44.0)
Number of Subjects Censored, n (%)	103 (73.6)	135 (56.0)
Time to first TEAE (months)		
25% percentile (95% CI)	2.04 (0.92, NE)	1.31 (0.72, 1.68)
Median (95% CI)	10.18 (NE, NE)	6.24 (4.60, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.0, 10.2	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.448 (0.194)
95% CI		(0.990, 2.118)
Log-rank p-value		0.056

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.6 (66.0, 81.2)	60.3 (54.0, 66.7)
6 months	70.7 (61.4, 79.9)	51.9 (44.4, 59.4)
9 months	70.7 (61.4, 79.9)	47.7 (39.5, 55.9)
12 months	0.0 (NE, NE)	41.7 (28.6, 54.8)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.61	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	25 (17.9)	69 (28.6)
Number of Subjects Censored, n (%)	115 (82.1)	172 (71.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.91, NE)	2.86 (1.61, 5.36)
Median (95% CI)	NE (NE, NE)	NE (9.43, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.368 (0.238)
95% CI		(0.858, 2.179)
Log-rank p-value		0.202

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.3 (74.7, 88.0)	73.9 (68.2, 79.7)
6 months	81.3 (74.7, 88.0)	68.8 (62.1, 75.5)
9 months	81.3 (74.7, 88.0)	65.6 (57.8, 73.4)
12 months	81.3 (74.7, 88.0)	61.2 (50.2, 72.2)
18 months	NE (NE, NE)	61.2 (50.2, 72.2)
Median Follow-up Time (months)	2.79	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	0	10 (4.1)
Number of Subjects Censored, n (%)	140 (100.0)	231 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.030

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.2 (92.3, 98.2)
6 months	100.0 (100.0, 100.0)	95.2 (92.3, 98.2)
9 months	100.0 (100.0, 100.0)	95.2 (92.3, 98.2)
12 months	100.0 (100.0, 100.0)	95.2 (92.3, 98.2)
18 months	NE (NE, NE)	95.2 (92.3, 98.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	2 (1.4)	9 (3.7)
Number of Subjects Censored, n (%)	138 (98.6)	232 (96.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.001 (0.794)
95% CI		(0.422, 9.490)
Log-rank p-value		0.375

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	96.4 (94.0, 98.9)
6 months	95.9 (89.4, 100.0)	95.6 (92.7, 98.5)
9 months	95.9 (89.4, 100.0)	95.6 (92.7, 98.5)
12 months	95.9 (89.4, 100.0)	95.6 (92.7, 98.5)
18 months	NE (NE, NE)	95.6 (92.7, 98.5)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	3 (2.1)	8 (3.3)
Number of Subjects Censored, n (%)	137 (97.9)	233 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.109 (0.691)
95% CI		(0.286, 4.301)
Log-rank p-value		0.790

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (94.7, 100.0)	96.9 (94.6, 99.2)
6 months	97.5 (94.7, 100.0)	96.9 (94.6, 99.2)
9 months	97.5 (94.7, 100.0)	93.3 (86.0, 100.0)
12 months	97.5 (94.7, 100.0)	93.3 (86.0, 100.0)
18 months	NE (NE, NE)	93.3 (86.0, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	1 (0.7)	9 (3.7)
Number of Subjects Censored, n (%)	139 (99.3)	232 (96.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.576 (1.064)
95% CI		(0.444, 28.778)
Log-rank p-value		0.221

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	96.9 (94.6, 99.2)
6 months	99.3 (97.8, 100.0)	95.6 (92.3, 98.9)
9 months	99.3 (97.8, 100.0)	93.2 (87.4, 98.9)
12 months	99.3 (97.8, 100.0)	93.2 (87.4, 98.9)
18 months	NE (NE, NE)	93.2 (87.4, 98.9)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	0	12 (5.0)
Number of Subjects Censored, n (%)	140 (100.0)	229 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.022

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.2 (93.7, 98.6)
6 months	100.0 (100.0, 100.0)	93.0 (88.7, 97.4)
9 months	100.0 (100.0, 100.0)	93.0 (88.7, 97.4)
12 months	100.0 (100.0, 100.0)	93.0 (88.7, 97.4)
18 months	NE (NE, NE)	93.0 (88.7, 97.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	3 (2.1)	10 (4.1)
Number of Subjects Censored, n (%)	137 (97.9)	231 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.371 (0.669)
95% CI		(0.370, 5.085)
Log-rank p-value		0.629

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (93.7, 100.0)	96.0 (93.4, 98.6)
6 months	97.1 (93.7, 100.0)	96.0 (93.4, 98.6)
9 months	97.1 (93.7, 100.0)	94.5 (90.5, 98.4)
12 months	97.1 (93.7, 100.0)	94.5 (90.5, 98.4)
18 months	NE (NE, NE)	94.5 (90.5, 98.4)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	1 (0.7)	9 (3.7)
Number of Subjects Censored, n (%)	139 (99.3)	232 (96.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.153 (1.080)
95% CI		(0.380, 26.160)
Log-rank p-value		0.236

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	97.8 (96.0, 99.7)
6 months	99.3 (97.8, 100.0)	95.8 (92.4, 99.3)
9 months	99.3 (97.8, 100.0)	90.8 (82.8, 98.8)
12 months	99.3 (97.8, 100.0)	90.8 (82.8, 98.8)
18 months	NE (NE, NE)	90.8 (82.8, 98.8)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	1 (0.7)	4 (1.7)
Number of Subjects Censored, n (%)	139 (99.3)	237 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Median (95% CI)	10.18 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 10.2	0.7, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.726 (1.141)
95% CI		(0.184, 16.160)
Log-rank p-value		0.705

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.3 (96.6, 100.0)
6 months	100.0 (100.0, 100.0)	98.3 (96.6, 100.0)
9 months	100.0 (100.0, 100.0)	98.3 (96.6, 100.0)
12 months	0.0 (NE, NE)	98.3 (96.6, 100.0)
18 months	0.0 (NE, NE)	98.3 (96.6, 100.0)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	1 (0.7)	7 (2.9)
Number of Subjects Censored, n (%)	139 (99.3)	234 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.006 (1.097)
95% CI		(0.234, 17.217)
Log-rank p-value		0.565

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.5, 100.0)	98.0 (96.1, 100.0)
6 months	99.1 (97.5, 100.0)	94.6 (90.2, 98.9)
9 months	99.1 (97.5, 100.0)	94.6 (90.2, 98.9)
12 months	99.1 (97.5, 100.0)	94.6 (90.2, 98.9)
18 months	NE (NE, NE)	94.6 (90.2, 98.9)
Median Follow-up Time (months)	2.83	4.01

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	41 (29.3)	98 (40.7)
Number of Subjects Censored, n (%)	99 (70.7)	143 (59.3)
Time to first TEAE (months)		
25% percentile (95% CI)	1.94 (1.05, 3.71)	1.61 (0.95, 1.97)
Median (95% CI)	5.82 (3.71, NE)	7.16 (5.78, NE)
75% percentile (95% CI)	5.82 (NE, NE)	NE (16.79, NE)
Min, Max	0.1, 5.8	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.173 (0.191)
95% CI		(0.807, 1.706)
Log-rank p-value		0.379

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.3 (63.4, 79.3)	63.4 (57.1, 69.7)
6 months	0.0 (NE, NE)	55.5 (48.1, 63.0)
9 months	0.0 (NE, NE)	49.4 (40.6, 58.3)
12 months	0.0 (NE, NE)	49.4 (40.6, 58.3)
18 months	0.0 (NE, NE)	32.9 (5.9, 59.9)
Median Follow-up Time (months)	2.71	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	16 (11.4)	32 (13.3)
Number of Subjects Censored, n (%)	124 (88.6)	209 (86.7)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (5.59, NE)	NE (6.47, NE)
Median (95% CI)	5.82 (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	5.82 (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 5.8	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.819 (0.320)
95% CI		(0.437, 1.535)
Log-rank p-value		0.409

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (81.2, 93.8)	88.7 (84.5, 92.9)
6 months	0.0 (NE, NE)	83.6 (77.7, 89.6)
9 months	0.0 (NE, NE)	80.2 (72.7, 87.6)
12 months	0.0 (NE, NE)	80.2 (72.7, 87.6)
18 months	0.0 (NE, NE)	80.2 (72.7, 87.6)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	8 (5.7)	24 (10.0)
Number of Subjects Censored, n (%)	132 (94.3)	217 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.3, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.219 (0.422)
95% CI		(0.533, 2.789)
Log-rank p-value		0.700

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.8 (91.0, 98.5)	92.6 (89.2, 96.0)
6 months	79.0 (50.5, 100.0)	88.3 (83.2, 93.3)
9 months	NE (NE, NE)	84.4 (77.1, 91.7)
12 months	NE (NE, NE)	84.4 (77.1, 91.7)
18 months	NE (NE, NE)	84.4 (77.1, 91.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	5 (3.6)	23 (9.5)
Number of Subjects Censored, n (%)	135 (96.4)	218 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.802 (0.508)
95% CI		(0.665, 4.882)
Log-rank p-value		0.261

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (94.2, 99.9)	93.1 (89.8, 96.4)
6 months	80.9 (51.8, 100.0)	90.1 (85.8, 94.4)
9 months	NE (NE, NE)	84.6 (77.2, 92.0)
12 months	NE (NE, NE)	84.6 (77.2, 92.0)
18 months	NE (NE, NE)	84.6 (77.2, 92.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	8 (5.7)	28 (11.6)
Number of Subjects Censored, n (%)	132 (94.3)	213 (88.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.495 (0.409)
95% CI		(0.671, 3.332)
Log-rank p-value		0.459

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.2 (90.2, 98.1)	90.8 (87.0, 94.5)
6 months	94.2 (90.2, 98.1)	86.1 (80.9, 91.2)
9 months	94.2 (90.2, 98.1)	83.9 (77.3, 90.4)
12 months	94.2 (90.2, 98.1)	83.9 (77.3, 90.4)
18 months	NE (NE, NE)	83.9 (77.3, 90.4)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	1 (0.7)	21 (8.7)
Number of Subjects Censored, n (%)	139 (99.3)	220 (91.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		10.464 (1.028)
95% CI		(1.395, 78.513)
Log-rank p-value		0.006

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.0, 100.0)	91.9 (88.2, 95.5)
6 months	99.0 (97.0, 100.0)	90.7 (86.5, 94.9)
9 months	99.0 (97.0, 100.0)	87.8 (82.1, 93.5)
12 months	99.0 (97.0, 100.0)	87.8 (82.1, 93.5)
18 months	NE (NE, NE)	87.8 (82.1, 93.5)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	5 (3.6)	15 (6.2)
Number of Subjects Censored, n (%)	135 (96.4)	226 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.416 (0.529)
95% CI		(0.502, 3.994)
Log-rank p-value		0.570

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.1 (92.7, 99.5)	94.3 (91.2, 97.3)
6 months	96.1 (92.7, 99.5)	92.9 (88.8, 96.9)
9 months	96.1 (92.7, 99.5)	91.4 (86.4, 96.3)
12 months	96.1 (92.7, 99.5)	91.4 (86.4, 96.3)
18 months	NE (NE, NE)	91.4 (86.4, 96.3)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	1 (0.7)	14 (5.8)
Number of Subjects Censored, n (%)	139 (99.3)	227 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	7.43 (NE, NE)	NE (NE, NE)
Median (95% CI)	7.43 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	7.43 (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 7.4	0.7*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.817 (1.049)
95% CI		(0.744, 45.503)
Log-rank p-value		0.058

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.0 (92.1, 97.9)
6 months	100.0 (100.0, 100.0)	92.4 (88.3, 96.5)
9 months	0.0 (NE, NE)	92.4 (88.3, 96.5)
12 months	0.0 (NE, NE)	92.4 (88.3, 96.5)
18 months	0.0 (NE, NE)	92.4 (88.3, 96.5)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	4 (2.9)	9 (3.7)
Number of Subjects Censored, n (%)	136 (97.1)	232 (96.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.897 (0.616)
95% CI		(0.268, 3.001)
Log-rank p-value		0.833

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (94.2, 100.0)	96.9 (94.7, 99.2)
6 months	93.0 (84.4, 100.0)	95.3 (92.1, 98.4)
9 months	93.0 (84.4, 100.0)	95.3 (92.1, 98.4)
12 months	93.0 (84.4, 100.0)	95.3 (92.1, 98.4)
18 months	NE (NE, NE)	95.3 (92.1, 98.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	0	7 (2.9)
Number of Subjects Censored, n (%)	140 (100.0)	234 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.072

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.3 (95.2, 99.4)
6 months	100.0 (100.0, 100.0)	96.4 (93.6, 99.2)
9 months	100.0 (100.0, 100.0)	96.4 (93.6, 99.2)
12 months	100.0 (100.0, 100.0)	96.4 (93.6, 99.2)
18 months	NE (NE, NE)	96.4 (93.6, 99.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	1 (0.7)	7 (2.9)
Number of Subjects Censored, n (%)	139 (99.3)	234 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.840 (1.071)
95% CI		(0.471, 31.306)
Log-rank p-value		0.171

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	96.9 (94.7, 99.2)
6 months	99.3 (97.8, 100.0)	96.9 (94.7, 99.2)
9 months	99.3 (97.8, 100.0)	96.9 (94.7, 99.2)
12 months	99.3 (97.8, 100.0)	96.9 (94.7, 99.2)
18 months	NE (NE, NE)	96.9 (94.7, 99.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	37 (26.4)	106 (44.0)
Number of Subjects Censored, n (%)	103 (73.6)	135 (56.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.91 (0.95, NE)	0.69 (0.46, 0.72)
Median (95% CI)	NE (NE, NE)	7.56 (4.30, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.683 (0.194)
95% CI		(1.150, 2.463)
Log-rank p-value		0.008

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.5 (63.6, 79.4)	61.0 (54.8, 67.2)
6 months	71.5 (63.6, 79.4)	54.3 (47.1, 61.4)
9 months	71.5 (63.6, 79.4)	49.0 (40.3, 57.7)
12 months	71.5 (63.6, 79.4)	37.9 (21.8, 54.0)
18 months	NE (NE, NE)	37.9 (21.8, 54.0)
Median Follow-up Time (months)	2.46	2.43

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	9 (6.4)	48 (19.9)
Number of Subjects Censored, n (%)	131 (93.6)	193 (80.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.61, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.374 (0.364)
95% CI		(1.652, 6.892)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.0 (88.4, 97.5)	79.9 (74.8, 85.0)
6 months	93.0 (88.4, 97.5)	79.9 (74.8, 85.0)
9 months	93.0 (88.4, 97.5)	79.9 (74.8, 85.0)
12 months	93.0 (88.4, 97.5)	79.9 (74.8, 85.0)
18 months	NE (NE, NE)	79.9 (74.8, 85.0)
Median Follow-up Time (months)	2.79	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	15 (10.7)	24 (10.0)
Number of Subjects Censored, n (%)	125 (89.3)	217 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	14.32 (10.28, NE)
Median (95% CI)	NE (NE, NE)	NE (14.32, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.641 (0.347)
95% CI		(0.325, 1.263)
Log-rank p-value		0.204

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.8 (83.4, 94.2)	93.0 (89.7, 96.4)
6 months	88.8 (83.4, 94.2)	89.8 (85.4, 94.3)
9 months	88.8 (83.4, 94.2)	86.9 (81.0, 92.8)
12 months	88.8 (83.4, 94.2)	81.1 (68.8, 93.4)
18 months	NE (NE, NE)	64.9 (34.8, 95.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	12 (8.6)	26 (10.8)
Number of Subjects Censored, n (%)	128 (91.4)	215 (89.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.144 (0.355)
95% CI		(0.570, 2.294)
Log-rank p-value		0.733

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.7 (85.6, 95.8)	89.7 (85.8, 93.7)
6 months	90.7 (85.6, 95.8)	89.7 (85.8, 93.7)
9 months	90.7 (85.6, 95.8)	88.2 (83.3, 93.1)
12 months	90.7 (85.6, 95.8)	78.4 (59.8, 97.0)
18 months	NE (NE, NE)	78.4 (59.8, 97.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	2 (1.4)	11 (4.6)
Number of Subjects Censored, n (%)	138 (98.6)	230 (95.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.146 (0.771)
95% CI		(0.694, 14.264)
Log-rank p-value		0.131

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.6, 100.0)	95.1 (92.3, 97.9)
6 months	98.6 (96.6, 100.0)	95.1 (92.3, 97.9)
9 months	98.6 (96.6, 100.0)	95.1 (92.3, 97.9)
12 months	98.6 (96.6, 100.0)	95.1 (92.3, 97.9)
18 months	NE (NE, NE)	95.1 (92.3, 97.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	2 (1.4)	5 (2.1)
Number of Subjects Censored, n (%)	138 (98.6)	236 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.364 (0.839)
95% CI		(0.263, 7.057)
Log-rank p-value		0.699

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.2, 100.0)	97.9 (96.1, 99.7)
6 months	98.4 (96.2, 100.0)	97.9 (96.1, 99.7)
9 months	98.4 (96.2, 100.0)	97.9 (96.1, 99.7)
12 months	98.4 (96.2, 100.0)	97.9 (96.1, 99.7)
18 months	NE (NE, NE)	97.9 (96.1, 99.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Vascular disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	19 (13.6)	84 (34.9)
Number of Subjects Censored, n (%)	121 (86.4)	157 (65.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.61, NE)	1.58 (0.89, 2.43)
Median (95% CI)	NE (NE, NE)	NE (7.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.7*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.441 (0.257)
95% CI		(1.476, 4.036)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Vascular disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.0 (79.8, 92.1)	66.3 (60.2, 72.5)
6 months	NE (NE, NE)	64.0 (57.3, 70.8)
9 months	NE (NE, NE)	54.4 (43.8, 65.1)
12 months	NE (NE, NE)	54.4 (43.8, 65.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.73	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	11 (7.9)	78 (32.4)
Number of Subjects Censored, n (%)	129 (92.1)	163 (67.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.61 (0.95, 2.79)
Median (95% CI)	NE (NE, NE)	NE (7.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.105 (0.324)
95% CI		(2.176, 7.743)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.2 (86.2, 96.3)	68.4 (62.3, 74.4)
6 months	91.2 (86.2, 96.3)	67.4 (61.2, 73.7)
9 months	NE (NE, NE)	58.0 (47.7, 68.3)
12 months	NE (NE, NE)	58.0 (47.7, 68.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	30 (21.4)	76 (31.5)
Number of Subjects Censored, n (%)	110 (78.6)	165 (68.5)
Time to first TEAE (months)		
25% percentile (95% CI)	3.71 (1.64, NE)	1.87 (0.99, 3.48)
Median (95% CI)	5.59 (5.59, NE)	NE (8.64, NE)
75% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Min, Max	0.0, 5.7*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.261 (0.219)
95% CI		(0.820, 1.938)
Log-rank p-value		0.283

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.5 (72.4, 86.6)	70.3 (64.3, 76.2)
6 months	NE (NE, NE)	65.4 (58.4, 72.4)
9 months	NE (NE, NE)	60.7 (49.8, 71.7)
12 months	NE (NE, NE)	54.0 (38.1, 69.8)
18 months	NE (NE, NE)	54.0 (38.1, 69.8)
Median Follow-up Time (months)	2.46	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	11 (7.9)	23 (9.5)
Number of Subjects Censored, n (%)	129 (92.1)	218 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.974 (0.375)
95% CI		(0.467, 2.033)
Log-rank p-value		0.897

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.9 (87.3, 96.5)	91.3 (87.6, 94.9)
6 months	91.9 (87.3, 96.5)	89.2 (84.6, 93.8)
9 months	91.9 (87.3, 96.5)	87.7 (82.3, 93.1)
12 months	91.9 (87.3, 96.5)	87.7 (82.3, 93.1)
18 months	NE (NE, NE)	87.7 (82.3, 93.1)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	7 (5.0)	21 (8.7)
Number of Subjects Censored, n (%)	133 (95.0)	220 (91.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.488 (0.442)
95% CI		(0.626, 3.538)
Log-rank p-value		0.312

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (92.0, 99.0)	91.7 (88.1, 95.3)
6 months	79.6 (51.0, 100.0)	89.7 (85.1, 94.3)
9 months	NE (NE, NE)	89.7 (85.1, 94.3)
12 months	NE (NE, NE)	89.7 (85.1, 94.3)
18 months	NE (NE, NE)	89.7 (85.1, 94.3)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	5 (3.6)	16 (6.6)
Number of Subjects Censored, n (%)	135 (96.4)	225 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.472 (0.523)
95% CI		(0.528, 4.099)
Log-rank p-value		0.365

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (95.0, 100.0)	93.4 (90.2, 96.7)
6 months	88.4 (75.9, 100.0)	92.2 (88.2, 96.2)
9 months	88.4 (75.9, 100.0)	92.2 (88.2, 96.2)
12 months	88.4 (75.9, 100.0)	92.2 (88.2, 96.2)
18 months	NE (NE, NE)	92.2 (88.2, 96.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	1 (0.7)	7 (2.9)
Number of Subjects Censored, n (%)	139 (99.3)	234 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.819 (1.072)
95% CI		(0.467, 31.242)
Log-rank p-value		0.198

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	96.8 (94.5, 99.2)
6 months	99.3 (97.8, 100.0)	96.8 (94.5, 99.2)
9 months	99.3 (97.8, 100.0)	96.8 (94.5, 99.2)
12 months	99.3 (97.8, 100.0)	96.8 (94.5, 99.2)
18 months	NE (NE, NE)	96.8 (94.5, 99.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	1 (0.7)	3 (1.2)
Number of Subjects Censored, n (%)	139 (99.3)	238 (98.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.336 (1.327)
95% CI		(0.025, 4.526)
Log-rank p-value		0.350

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	100.0 (100.0, 100.0)
6 months	99.3 (97.8, 100.0)	100.0 (100.0, 100.0)
9 months	99.3 (97.8, 100.0)	91.7 (82.4, 100.0)
12 months	99.3 (97.8, 100.0)	91.7 (82.4, 100.0)
18 months	NE (NE, NE)	91.7 (82.4, 100.0)
Median Follow-up Time (months)	2.83	4.11

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	0	4 (1.7)
Number of Subjects Censored, n (%)	140 (100.0)	237 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.235

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.0 (96.1, 100.0)
6 months	100.0 (100.0, 100.0)	98.0 (96.1, 100.0)
9 months	100.0 (100.0, 100.0)	98.0 (96.1, 100.0)
12 months	100.0 (100.0, 100.0)	98.0 (96.1, 100.0)
18 months	NE (NE, NE)	98.0 (96.1, 100.0)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	13 (9.3)	84 (34.9)
Number of Subjects Censored, n (%)	127 (90.7)	157 (65.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.51 (0.95, 1.87)
Median (95% CI)	NE (NE, NE)	13.14 (13.14, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.14, NE)
Min, Max	0.1, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.794 (0.301)
95% CI		(2.104, 6.841)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.5 (85.5, 95.4)	66.9 (60.8, 73.0)
6 months	90.5 (85.5, 95.4)	60.9 (53.7, 68.2)
9 months	90.5 (85.5, 95.4)	60.9 (53.7, 68.2)
12 months	90.5 (85.5, 95.4)	60.9 (53.7, 68.2)
18 months	NE (NE, NE)	40.6 (7.8, 73.5)
Median Follow-up Time (months)	2.79	2.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	3 (2.1)	41 (17.0)
Number of Subjects Censored, n (%)	137 (97.9)	200 (83.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.86, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		7.382 (0.600)
95% CI		(2.278, 23.926)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.4, 100.0)	84.6 (80.0, 89.3)
6 months	97.8 (95.4, 100.0)	79.9 (73.9, 85.9)
9 months	97.8 (95.4, 100.0)	79.9 (73.9, 85.9)
12 months	97.8 (95.4, 100.0)	79.9 (73.9, 85.9)
18 months	NE (NE, NE)	79.9 (73.9, 85.9)
Median Follow-up Time (months)	2.83	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	5 (3.6)	9 (3.7)
Number of Subjects Censored, n (%)	135 (96.4)	232 (96.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.936 (0.564)
95% CI		(0.310, 2.826)
Log-rank p-value		0.857

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.4 (93.2, 99.5)	96.0 (93.4, 98.6)
6 months	96.4 (93.2, 99.5)	96.0 (93.4, 98.6)
9 months	96.4 (93.2, 99.5)	96.0 (93.4, 98.6)
12 months	96.4 (93.2, 99.5)	96.0 (93.4, 98.6)
18 months	NE (NE, NE)	96.0 (93.4, 98.6)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	1 (0.7)	8 (3.3)
Number of Subjects Censored, n (%)	139 (99.3)	233 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.801 (1.065)
95% CI		(0.596, 38.696)
Log-rank p-value		0.102

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.5, 100.0)	96.6 (94.3, 98.9)
6 months	99.1 (97.5, 100.0)	96.6 (94.3, 98.9)
9 months	99.1 (97.5, 100.0)	96.6 (94.3, 98.9)
12 months	99.1 (97.5, 100.0)	96.6 (94.3, 98.9)
18 months	NE (NE, NE)	96.6 (94.3, 98.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Nervous system disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	19 (13.6)	51 (21.2)
Number of Subjects Censored, n (%)	121 (86.4)	190 (78.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	6.11 (3.98, NE)
Median (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.345 (0.274)
95% CI		(0.787, 2.299)
Log-rank p-value		0.305

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Nervous system disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.3 (79.1, 91.5)	81.7 (76.7, 86.7)
6 months	85.3 (79.1, 91.5)	76.3 (70.0, 82.6)
9 months	85.3 (79.1, 91.5)	74.7 (67.8, 81.6)
12 months	85.3 (79.1, 91.5)	74.7 (67.8, 81.6)
18 months	NE (NE, NE)	74.7 (67.8, 81.6)
Median Follow-up Time (months)	2.78	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	4 (2.9)	16 (6.6)
Number of Subjects Censored, n (%)	136 (97.1)	225 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
Median (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.971 (0.570)
95% CI		(0.645, 6.028)
Log-rank p-value		0.227

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (93.8, 99.9)	94.5 (91.6, 97.4)
6 months	96.9 (93.8, 99.9)	93.5 (90.1, 97.0)
9 months	96.9 (93.8, 99.9)	91.9 (87.3, 96.5)
12 months	96.9 (93.8, 99.9)	91.9 (87.3, 96.5)
18 months	NE (NE, NE)	91.9 (87.3, 96.5)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	5 (3.6)	7 (2.9)
Number of Subjects Censored, n (%)	135 (96.4)	234 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.792 (0.587)
95% CI		(0.251, 2.500)
Log-rank p-value		0.672

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.3 (93.2, 99.5)	97.0 (94.9, 99.2)
6 months	96.3 (93.2, 99.5)	97.0 (94.9, 99.2)
9 months	96.3 (93.2, 99.5)	97.0 (94.9, 99.2)
12 months	96.3 (93.2, 99.5)	97.0 (94.9, 99.2)
18 months	NE (NE, NE)	97.0 (94.9, 99.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	2 (1.4)	5 (2.1)
Number of Subjects Censored, n (%)	138 (98.6)	236 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.200 (0.843)
95% CI		(0.230, 6.266)
Log-rank p-value		0.873

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.3, 100.0)	97.9 (96.1, 99.7)
6 months	98.4 (96.3, 100.0)	97.9 (96.1, 99.7)
9 months	98.4 (96.3, 100.0)	97.9 (96.1, 99.7)
12 months	98.4 (96.3, 100.0)	97.9 (96.1, 99.7)
18 months	NE (NE, NE)	97.9 (96.1, 99.7)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	21 (15.0)	57 (23.7)
Number of Subjects Censored, n (%)	119 (85.0)	184 (76.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.94 (2.76, NE)
Median (95% CI)	NE (NE, NE)	13.60 (13.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.2*, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.233 (0.262)
95% CI		(0.737, 2.061)
Log-rank p-value		0.394

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.2 (76.5, 89.9)	80.1 (74.9, 85.3)
6 months	83.2 (76.5, 89.9)	73.4 (66.7, 80.0)
9 months	83.2 (76.5, 89.9)	69.4 (61.1, 77.7)
12 months	83.2 (76.5, 89.9)	69.4 (61.1, 77.7)
18 months	NE (NE, NE)	46.3 (8.8, 83.7)
Median Follow-up Time (months)	2.73	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	8 (5.7)	39 (16.2)
Number of Subjects Censored, n (%)	132 (94.3)	202 (83.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.60 (5.78, NE)
Median (95% CI)	NE (NE, NE)	NE (13.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.2*, 13.0*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.228 (0.395)
95% CI		(1.026, 4.835)
Log-rank p-value		0.036

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.0 (89.9, 98.0)	86.5 (82.1, 91.0)
6 months	94.0 (89.9, 98.0)	81.4 (75.4, 87.3)
9 months	94.0 (89.9, 98.0)	79.0 (71.6, 86.4)
12 months	94.0 (89.9, 98.0)	79.0 (71.6, 86.4)
18 months	NE (NE, NE)	52.6 (10.2, 95.1)
Median Follow-up Time (months)	2.79	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	3 (2.1)	6 (2.5)
Number of Subjects Censored, n (%)	137 (97.9)	235 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.899 (0.715)
95% CI		(0.221, 3.652)
Log-rank p-value		0.840

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (95.1, 100.0)	97.9 (96.0, 99.7)
6 months	97.7 (95.1, 100.0)	97.0 (94.6, 99.5)
9 months	97.7 (95.1, 100.0)	97.0 (94.6, 99.5)
12 months	97.7 (95.1, 100.0)	97.0 (94.6, 99.5)
18 months	NE (NE, NE)	97.0 (94.6, 99.5)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Infections and infestations**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	15 (10.7)	46 (19.1)
Number of Subjects Censored, n (%)	125 (89.3)	195 (80.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	5.78 (3.81, NE)
Median (95% CI)	NE (NE, NE)	NE (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.107 (0.310)
95% CI		(0.602, 2.033)
Log-rank p-value		0.779

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Infections and infestations**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (84.8, 95.2)	86.3 (81.7, 91.0)
6 months	78.1 (60.5, 95.8)	74.2 (66.6, 81.8)
9 months	78.1 (60.5, 95.8)	70.5 (61.7, 79.3)
12 months	78.1 (60.5, 95.8)	62.6 (46.2, 79.1)
18 months	NE (NE, NE)	62.6 (46.2, 79.1)
Median Follow-up Time (months)	2.79	3.52

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	4 (2.9)	5 (2.1)
Number of Subjects Censored, n (%)	136 (97.1)	236 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.14, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.2, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.363 (0.722)
95% CI		(0.088, 1.491)
Log-rank p-value		0.211

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.6, 100.0)	98.7 (97.3, 100.0)
6 months	88.1 (73.0, 100.0)	96.6 (93.3, 99.9)
9 months	88.1 (73.0, 100.0)	96.6 (93.3, 99.9)
12 months	88.1 (73.0, 100.0)	96.6 (93.3, 99.9)
18 months	NE (NE, NE)	96.6 (93.3, 99.9)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	4 (2.9)	6 (2.5)
Number of Subjects Censored, n (%)	136 (97.1)	235 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (11.56, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.327 (0.705)
95% CI		(0.082, 1.301)
Log-rank p-value		0.076

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.3, 100.0)	99.5 (98.5, 100.0)
6 months	90.3 (75.9, 100.0)	96.9 (93.9, 100.0)
9 months	90.3 (75.9, 100.0)	95.3 (90.8, 99.7)
12 months	90.3 (75.9, 100.0)	85.7 (67.6, 100.0)
18 months	NE (NE, NE)	85.7 (67.6, 100.0)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	1 (0.7)	8 (3.3)
Number of Subjects Censored, n (%)	139 (99.3)	233 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.306 (1.065)
95% CI		(0.410, 26.678)
Log-rank p-value		0.242

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	96.1 (93.4, 98.8)
6 months	99.3 (97.8, 100.0)	96.1 (93.4, 98.8)
9 months	99.3 (97.8, 100.0)	96.1 (93.4, 98.8)
12 months	99.3 (97.8, 100.0)	96.1 (93.4, 98.8)
18 months	NE (NE, NE)	96.1 (93.4, 98.8)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	24 (17.1)	35 (14.5)
Number of Subjects Censored, n (%)	116 (82.9)	206 (85.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.79, NE)	NE (5.85, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.671 (0.272)
95% CI		(0.394, 1.144)
Log-rank p-value		0.153

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.8 (73.7, 87.9)	86.9 (82.5, 91.3)
6 months	80.8 (73.7, 87.9)	81.9 (75.7, 88.0)
9 months	80.8 (73.7, 87.9)	81.9 (75.7, 88.0)
12 months	80.8 (73.7, 87.9)	81.9 (75.7, 88.0)
18 months	NE (NE, NE)	81.9 (75.7, 88.0)
Median Follow-up Time (months)	2.78	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	18 (12.9)	17 (7.1)
Number of Subjects Censored, n (%)	122 (87.1)	224 (92.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	17.74 (17.74, NE)
Median (95% CI)	NE (NE, NE)	17.74 (17.74, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.74, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.325 (0.365)
95% CI		(0.159, 0.664)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.7 (78.1, 91.4)	95.1 (92.3, 98.0)
6 months	84.7 (78.1, 91.4)	89.9 (84.6, 95.3)
9 months	84.7 (78.1, 91.4)	89.9 (84.6, 95.3)
12 months	84.7 (78.1, 91.4)	89.9 (84.6, 95.3)
18 months	NE (NE, NE)	45.0 (0.0, 100.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	3 (2.1)	19 (7.9)
Number of Subjects Censored, n (%)	137 (97.9)	222 (92.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.508 (0.623)
95% CI		(1.035, 11.892)
Log-rank p-value		0.032

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (95.1, 100.0)	91.7 (88.1, 95.3)
6 months	97.7 (95.1, 100.0)	91.7 (88.1, 95.3)
9 months	97.7 (95.1, 100.0)	91.7 (88.1, 95.3)
12 months	97.7 (95.1, 100.0)	91.7 (88.1, 95.3)
18 months	NE (NE, NE)	91.7 (88.1, 95.3)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Endocrine disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	0	43 (17.8)
Number of Subjects Censored, n (%)	140 (100.0)	198 (82.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	6.90 (4.37, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Endocrine disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	87.2 (82.8, 91.5)
6 months	100.0 (100.0, 100.0)	75.3 (67.8, 82.9)
9 months	100.0 (100.0, 100.0)	73.0 (64.5, 81.6)
12 months	100.0 (100.0, 100.0)	67.4 (54.2, 80.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.48

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	0	40 (16.6)
Number of Subjects Censored, n (%)	140 (100.0)	201 (83.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	7.33 (5.52, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	88.5 (84.3, 92.7)
6 months	100.0 (100.0, 100.0)	77.6 (70.3, 84.9)
9 months	100.0 (100.0, 100.0)	72.8 (63.3, 82.2)
12 months	100.0 (100.0, 100.0)	67.2 (53.5, 80.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	10 (7.1)	34 (14.1)
Number of Subjects Censored, n (%)	130 (92.9)	207 (85.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.29, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.402 (0.368)
95% CI		(0.682, 2.886)
Log-rank p-value		0.385

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (88.4, 97.4)	88.7 (84.4, 92.9)
6 months	90.0 (82.9, 97.1)	80.6 (74.0, 87.1)
9 months	90.0 (82.9, 97.1)	80.6 (74.0, 87.1)
12 months	90.0 (82.9, 97.1)	80.6 (74.0, 87.1)
18 months	NE (NE, NE)	80.6 (74.0, 87.1)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	6 (4.3)	15 (6.2)
Number of Subjects Censored, n (%)	134 (95.7)	226 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.015 (0.489)
95% CI		(0.389, 2.646)
Log-rank p-value		0.993

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (91.7, 99.0)	94.2 (91.0, 97.4)
6 months	95.4 (91.7, 99.0)	91.5 (87.0, 95.9)
9 months	95.4 (91.7, 99.0)	91.5 (87.0, 95.9)
12 months	95.4 (91.7, 99.0)	91.5 (87.0, 95.9)
18 months	NE (NE, NE)	91.5 (87.0, 95.9)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	1 (0.7)	5 (2.1)
Number of Subjects Censored, n (%)	139 (99.3)	236 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.531 (1.119)
95% CI		(0.282, 22.703)
Log-rank p-value		0.460

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.7 (95.6, 99.7)
6 months	96.9 (90.8, 100.0)	97.7 (95.6, 99.7)
9 months	96.9 (90.8, 100.0)	97.7 (95.6, 99.7)
12 months	96.9 (90.8, 100.0)	97.7 (95.6, 99.7)
18 months	NE (NE, NE)	97.7 (95.6, 99.7)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	2 (1.4)	9 (3.7)
Number of Subjects Censored, n (%)	138 (98.6)	232 (96.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.787 (0.799)
95% CI		(0.373, 8.548)
Log-rank p-value		0.458

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (95.8, 100.0)	96.9 (94.6, 99.2)
6 months	98.3 (95.8, 100.0)	94.9 (91.3, 98.5)
9 months	98.3 (95.8, 100.0)	94.9 (91.3, 98.5)
12 months	98.3 (95.8, 100.0)	94.9 (91.3, 98.5)
18 months	NE (NE, NE)	94.9 (91.3, 98.5)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	13 (9.3)	34 (14.1)
Number of Subjects Censored, n (%)	127 (90.7)	207 (85.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.62, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.4, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.221 (0.332)
95% CI		(0.638, 2.340)
Log-rank p-value		0.573

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.2 (86.4, 95.9)	86.6 (82.1, 91.1)
6 months	88.1 (80.7, 95.6)	84.6 (79.4, 89.8)
9 months	88.1 (80.7, 95.6)	82.2 (75.3, 89.1)
12 months	88.1 (80.7, 95.6)	77.9 (67.4, 88.4)
18 months	NE (NE, NE)	77.9 (67.4, 88.4)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	0	14 (5.8)
Number of Subjects Censored, n (%)	140 (100.0)	227 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.66, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.013

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.4 (91.2, 97.5)
6 months	100.0 (100.0, 100.0)	93.0 (89.0, 97.0)
9 months	100.0 (100.0, 100.0)	93.0 (89.0, 97.0)
12 months	100.0 (100.0, 100.0)	88.1 (78.1, 98.2)
18 months	NE (NE, NE)	88.1 (78.1, 98.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Number of Subjects with Events, n (%)	1 (0.7)	9 (3.7)
Number of Subjects Censored, n (%)	139 (99.3)	232 (96.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.492 (1.066)
95% CI		(0.432, 28.232)
Log-rank p-value		0.235

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Male

Statistics	Placebo + BSC N=140	Fruquintinib + BSC N=241
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	96.9 (94.7, 99.2)
6 months	99.3 (97.8, 100.0)	96.1 (93.4, 98.9)
9 months	99.3 (97.8, 100.0)	93.6 (88.1, 99.2)
12 months	99.3 (97.8, 100.0)	93.6 (88.1, 99.2)
18 months	NE (NE, NE)	93.6 (88.1, 99.2)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	49 (54.4)	148 (68.8)
Number of Subjects Censored, n (%)	41 (45.6)	67 (31.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.53, 0.76)	0.46 (0.26, 0.69)
Median (95% CI)	1.94 (1.18, NE)	1.35 (0.72, 1.71)
75% percentile (95% CI)	NE (NE, NE)	5.55 (4.21, NE)
Min, Max	0.0, 6.8*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.335 (0.166)
95% CI		(0.963, 1.849)
Log-rank p-value		0.107

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	44.1 (33.3, 54.9)	37.5 (30.9, 44.1)
6 months	41.0 (29.3, 52.6)	24.8 (17.9, 31.7)
9 months	NE (NE, NE)	22.7 (15.3, 30.1)
12 months	NE (NE, NE)	22.7 (15.3, 30.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.66	1.28

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	21 (23.3)	74 (34.4)
Number of Subjects Censored, n (%)	69 (76.7)	141 (65.6)
Time to first TEAE (months)		
25% percentile (95% CI)	3.22 (0.72, NE)	1.61 (0.72, 2.56)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.390 (0.249)
95% CI		(0.854, 2.263)
Log-rank p-value		0.196

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.2 (68.4, 86.0)	66.6 (60.0, 73.1)
6 months	72.9 (61.2, 84.6)	62.0 (54.7, 69.3)
9 months	NE (NE, NE)	62.0 (54.7, 69.3)
12 months	NE (NE, NE)	62.0 (54.7, 69.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.27	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	14 (15.6)	39 (18.1)
Number of Subjects Censored, n (%)	76 (84.4)	176 (81.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.87, NE)	NE (4.60, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.117 (0.317)
95% CI		(0.600, 2.079)
Log-rank p-value		0.801

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.7 (75.8, 91.5)	83.9 (78.9, 88.8)
6 months	83.7 (75.8, 91.5)	79.1 (72.9, 85.4)
9 months	NE (NE, NE)	79.1 (72.9, 85.4)
12 months	NE (NE, NE)	79.1 (72.9, 85.4)
18 months	NE (NE, NE)	79.1 (72.9, 85.4)
Median Follow-up Time (months)	2.74	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	8 (8.9)	17 (7.9)
Number of Subjects Censored, n (%)	82 (91.1)	198 (92.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.762 (0.436)
95% CI		(0.324, 1.789)
Log-rank p-value		0.484

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.6 (84.3, 96.8)	92.9 (89.4, 96.3)
6 months	90.6 (84.3, 96.8)	90.9 (86.4, 95.3)
9 months	NE (NE, NE)	90.9 (86.4, 95.3)
12 months	NE (NE, NE)	90.9 (86.4, 95.3)
18 months	NE (NE, NE)	90.9 (86.4, 95.3)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	3 (3.3)	34 (15.8)
Number of Subjects Censored, n (%)	87 (96.7)	181 (84.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.26, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.1, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.314 (0.604)
95% CI		(1.320, 14.092)
Log-rank p-value		0.007

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.6 (92.7, 100.0)	85.6 (80.9, 90.4)
6 months	96.6 (92.7, 100.0)	82.8 (77.2, 88.4)
9 months	NE (NE, NE)	80.5 (73.4, 87.6)
12 months	NE (NE, NE)	80.5 (73.4, 87.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	9 (10.0)	12 (5.6)
Number of Subjects Censored, n (%)	81 (90.0)	203 (94.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.382 (0.459)
95% CI		(0.155, 0.940)
Log-rank p-value		0.026

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.2 (80.8, 95.6)	96.4 (93.8, 99.0)
6 months	88.2 (80.8, 95.6)	92.3 (87.6, 97.1)
9 months	NE (NE, NE)	92.3 (87.6, 97.1)
12 months	NE (NE, NE)	92.3 (87.6, 97.1)
18 months	NE (NE, NE)	76.9 (49.1, 100.0)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	7 (7.8)	13 (6.0)
Number of Subjects Censored, n (%)	83 (92.2)	202 (94.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.692 (0.471)
95% CI		(0.275, 1.743)
Log-rank p-value		0.429

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.1 (86.4, 97.7)	93.7 (90.3, 97.0)
6 months	92.1 (86.4, 97.7)	93.7 (90.3, 97.0)
9 months	NE (NE, NE)	93.7 (90.3, 97.0)
12 months	NE (NE, NE)	93.7 (90.3, 97.0)
18 months	NE (NE, NE)	93.7 (90.3, 97.0)
Median Follow-up Time (months)	2.83	3.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	2 (2.2)	8 (3.7)
Number of Subjects Censored, n (%)	88 (97.8)	207 (96.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.72, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.872 (0.844)
95% CI		(0.167, 4.559)
Log-rank p-value		0.767

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (94.7, 100.0)	98.1 (96.3, 99.9)
6 months	97.8 (94.7, 100.0)	97.0 (94.2, 99.8)
9 months	NE (NE, NE)	94.6 (89.1, 100.0)
12 months	NE (NE, NE)	85.1 (71.5, 98.8)
18 months	NE (NE, NE)	85.1 (71.5, 98.8)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	3 (3.3)	7 (3.3)
Number of Subjects Censored, n (%)	87 (96.7)	208 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 8.4*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.732 (0.707)
95% CI		(0.183, 2.928)
Log-rank p-value		0.587

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (90.4, 100.0)	97.5 (95.3, 99.7)
6 months	95.5 (90.4, 100.0)	96.5 (93.6, 99.4)
9 months	NE (NE, NE)	94.1 (88.6, 99.5)
12 months	NE (NE, NE)	94.1 (88.6, 99.5)
18 months	NE (NE, NE)	94.1 (88.6, 99.5)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	1 (1.1)	4 (1.9)
Number of Subjects Censored, n (%)	89 (98.9)	211 (98.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.238 (1.136)
95% CI		(0.134, 11.472)
Log-rank p-value		0.902

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.7, 100.0)	98.6 (97.0, 100.0)
6 months	98.9 (96.7, 100.0)	97.7 (95.4, 100.0)
9 months	NE (NE, NE)	97.7 (95.4, 100.0)
12 months	NE (NE, NE)	97.7 (95.4, 100.0)
18 months	NE (NE, NE)	97.7 (95.4, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	53 (58.9)	145 (67.4)
Number of Subjects Censored, n (%)	37 (41.1)	70 (32.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.59 (0.36, 0.69)	0.46 (0.39, 0.69)
Median (95% CI)	1.54 (0.89, 3.75)	1.64 (0.95, 2.46)
75% percentile (95% CI)	5.36 (4.34, NE)	5.55 (4.40, NE)
Min, Max	0.0, 6.4*	0.0, 11.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.069 (0.164)
95% CI		(0.775, 1.475)
Log-rank p-value		0.586

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	41.7 (31.0, 52.4)	41.2 (34.4, 47.9)
6 months	24.9 (7.5, 42.3)	22.9 (15.5, 30.4)
9 months	NE (NE, NE)	20.9 (13.0, 28.7)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.20	1.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	6 (6.7)	50 (23.3)
Number of Subjects Censored, n (%)	84 (93.3)	165 (76.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.95 (2.20, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 6.8*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.115 (0.434)
95% CI		(1.329, 7.299)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.2 (87.9, 98.5)	79.5 (74.0, 85.0)
6 months	93.2 (87.9, 98.5)	74.0 (67.1, 81.0)
9 months	NE (NE, NE)	70.1 (61.6, 78.6)
12 months	NE (NE, NE)	70.1 (61.6, 78.6)
18 months	NE (NE, NE)	70.1 (61.6, 78.6)
Median Follow-up Time (months)	2.78	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	21 (23.3)	38 (17.7)
Number of Subjects Censored, n (%)	69 (76.7)	177 (82.3)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (0.76, NE)	8.31 (5.29, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.622 (0.284)
95% CI		(0.356, 1.085)
Log-rank p-value		0.103

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.5 (67.3, 85.7)	85.3 (80.3, 90.3)
6 months	71.0 (57.6, 84.4)	80.1 (73.6, 86.6)
9 months	NE (NE, NE)	74.7 (66.0, 83.3)
12 months	NE (NE, NE)	71.1 (60.4, 81.8)
18 months	NE (NE, NE)	71.1 (60.4, 81.8)
Median Follow-up Time (months)	2.56	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	16 (17.8)	40 (18.6)
Number of Subjects Censored, n (%)	74 (82.2)	175 (81.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.64, NE)	7.98 (4.83, 12.25)
Median (95% CI)	NE (NE, NE)	12.25 (10.12, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (12.25, NE)
Min, Max	0.1, 6.8*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.879 (0.314)
95% CI		(0.475, 1.625)
Log-rank p-value		0.637

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.7 (72.1, 89.3)	86.3 (81.6, 91.1)
6 months	80.7 (72.1, 89.3)	79.3 (72.6, 86.0)
9 months	NE (NE, NE)	73.2 (64.0, 82.4)
12 months	NE (NE, NE)	66.6 (51.6, 81.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.64	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	10 (11.1)	35 (16.3)
Number of Subjects Censored, n (%)	80 (88.9)	180 (83.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.70, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.183 (0.363)
95% CI		(0.580, 2.411)
Log-rank p-value		0.727

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.3 (81.4, 95.2)	86.1 (81.3, 90.9)
6 months	88.3 (81.4, 95.2)	79.0 (72.2, 85.8)
9 months	NE (NE, NE)	79.0 (72.2, 85.8)
12 months	NE (NE, NE)	79.0 (72.2, 85.8)
18 months	NE (NE, NE)	79.0 (72.2, 85.8)
Median Follow-up Time (months)	2.74	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	16 (17.8)	41 (19.1)
Number of Subjects Censored, n (%)	74 (82.2)	174 (80.9)
Time to first TEAE (months)		
25% percentile (95% CI)	5.36 (1.97, NE)	7.10 (4.21, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.894 (0.303)
95% CI		(0.494, 1.618)
Log-rank p-value		0.748

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.8 (73.3, 90.2)	85.8 (81.0, 90.6)
6 months	74.3 (58.5, 90.2)	78.0 (71.2, 84.9)
9 months	NE (NE, NE)	72.8 (64.1, 81.4)
12 months	NE (NE, NE)	67.2 (54.0, 80.4)
18 months	NE (NE, NE)	67.2 (54.0, 80.4)
Median Follow-up Time (months)	2.73	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	3 (3.3)	32 (14.9)
Number of Subjects Censored, n (%)	87 (96.7)	183 (85.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.87, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.247 (0.732)
95% CI		(1.487, 26.244)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.5 (92.5, 100.0)	87.6 (83.2, 92.1)
6 months	96.5 (92.5, 100.0)	84.0 (78.5, 89.6)
9 months	NE (NE, NE)	79.9 (72.2, 87.6)
12 months	NE (NE, NE)	79.9 (72.2, 87.6)
18 months	NE (NE, NE)	79.9 (72.2, 87.6)
Median Follow-up Time (months)	2.83	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	0	20 (9.3)
Number of Subjects Censored, n (%)	90 (100.0)	195 (90.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.013

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	92.1 (88.4, 95.8)
6 months	100.0 (100.0, 100.0)	88.0 (82.6, 93.3)
9 months	NE (NE, NE)	88.0 (82.6, 93.3)
12 months	NE (NE, NE)	88.0 (82.6, 93.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	1 (1.1)	4 (1.9)
Number of Subjects Censored, n (%)	89 (98.9)	211 (98.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.425 (1.149)
95% CI		(0.150, 13.543)
Log-rank p-value		0.775

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.7, 100.0)	98.6 (97.0, 100.0)
6 months	98.9 (96.7, 100.0)	97.3 (94.3, 100.0)
9 months	NE (NE, NE)	97.3 (94.3, 100.0)
12 months	NE (NE, NE)	97.3 (94.3, 100.0)
18 months	NE (NE, NE)	97.3 (94.3, 100.0)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	1 (1.1)	5 (2.3)
Number of Subjects Censored, n (%)	89 (98.9)	210 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.475 (1.122)
95% CI		(0.164, 13.289)
Log-rank p-value		0.725

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.7, 100.0)	97.6 (95.6, 99.7)
6 months	98.9 (96.7, 100.0)	97.6 (95.6, 99.7)
9 months	NE (NE, NE)	97.6 (95.6, 99.7)
12 months	NE (NE, NE)	97.6 (95.6, 99.7)
18 months	NE (NE, NE)	97.6 (95.6, 99.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	5 (5.6)	3 (1.4)
Number of Subjects Censored, n (%)	85 (94.4)	212 (98.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.189 (0.761)
95% CI		(0.042, 0.837)
Log-rank p-value		0.021

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.1 (89.1, 99.1)	99.0 (97.6, 100.0)
6 months	94.1 (89.1, 99.1)	97.6 (94.7, 100.0)
9 months	NE (NE, NE)	97.6 (94.7, 100.0)
12 months	NE (NE, NE)	97.6 (94.7, 100.0)
18 months	NE (NE, NE)	97.6 (94.7, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	0	7 (3.3)
Number of Subjects Censored, n (%)	90 (100.0)	208 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.078

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.0 (94.7, 99.4)
6 months	100.0 (100.0, 100.0)	97.0 (94.7, 99.4)
9 months	NE (NE, NE)	94.3 (88.6, 100.0)
12 months	NE (NE, NE)	94.3 (88.6, 100.0)
18 months	NE (NE, NE)	94.3 (88.6, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	26 (28.9)	90 (41.9)
Number of Subjects Censored, n (%)	64 (71.1)	125 (58.1)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.69, NE)	1.45 (0.95, 1.87)
Median (95% CI)	NE (4.27, NE)	8.02 (3.94, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.294 (0.228)
95% CI		(0.827, 2.025)
Log-rank p-value		0.278

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.1 (61.5, 80.7)	60.1 (53.2, 67.0)
6 months	64.7 (49.7, 79.6)	54.4 (46.8, 62.1)
9 months	NE (NE, NE)	49.4 (40.4, 58.3)
12 months	NE (NE, NE)	49.4 (40.4, 58.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.28	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	15 (16.7)	55 (25.6)
Number of Subjects Censored, n (%)	75 (83.3)	160 (74.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.87, NE)	2.99 (1.71, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.483 (0.302)
95% CI		(0.821, 2.681)
Log-rank p-value		0.168

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.3 (75.2, 91.3)	74.5 (68.3, 80.7)
6 months	77.3 (63.8, 90.8)	72.0 (65.5, 78.6)
9 months	NE (NE, NE)	70.6 (63.6, 77.6)
12 months	NE (NE, NE)	70.6 (63.6, 77.6)
18 months	NE (NE, NE)	70.6 (63.6, 77.6)
Median Follow-up Time (months)	2.58	2.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	4 (4.4)	18 (8.4)
Number of Subjects Censored, n (%)	86 (95.6)	197 (91.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.523 (0.558)
95% CI		(0.511, 4.545)
Log-rank p-value		0.459

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (91.2, 99.8)	92.6 (88.9, 96.2)
6 months	95.5 (91.2, 99.8)	90.7 (86.4, 95.1)
9 months	NE (NE, NE)	88.5 (82.4, 94.6)
12 months	NE (NE, NE)	88.5 (82.4, 94.6)
18 months	NE (NE, NE)	88.5 (82.4, 94.6)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	3 (3.3)	11 (5.1)
Number of Subjects Censored, n (%)	87 (96.7)	204 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 6.8*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.051 (0.669)
95% CI		(0.283, 3.900)
Log-rank p-value		0.998

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.6 (92.8, 100.0)	96.5 (94.0, 99.1)
6 months	96.6 (92.8, 100.0)	93.2 (88.8, 97.7)
9 months	NE (NE, NE)	91.2 (85.3, 97.1)
12 months	NE (NE, NE)	91.2 (85.3, 97.1)
18 months	NE (NE, NE)	91.2 (85.3, 97.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	1 (1.1)	6 (2.8)
Number of Subjects Censored, n (%)	89 (98.9)	209 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 6.8*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.132 (1.098)
95% CI		(0.248, 18.337)
Log-rank p-value		0.498

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.7, 100.0)	97.5 (95.4, 99.7)
6 months	98.9 (96.7, 100.0)	96.7 (94.0, 99.4)
9 months	NE (NE, NE)	96.7 (94.0, 99.4)
12 months	NE (NE, NE)	96.7 (94.0, 99.4)
18 months	NE (NE, NE)	96.7 (94.0, 99.4)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	2 (2.2)	6 (2.8)
Number of Subjects Censored, n (%)	88 (97.8)	209 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.986 (0.821)
95% CI		(0.197, 4.931)
Log-rank p-value		0.979

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (94.6, 100.0)	97.0 (94.7, 99.4)
6 months	97.7 (94.6, 100.0)	97.0 (94.7, 99.4)
9 months	NE (NE, NE)	97.0 (94.7, 99.4)
12 months	NE (NE, NE)	97.0 (94.7, 99.4)
18 months	NE (NE, NE)	97.0 (94.7, 99.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	0	6 (2.8)
Number of Subjects Censored, n (%)	90 (100.0)	209 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.190

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.5 (95.3, 99.7)
6 months	100.0 (100.0, 100.0)	97.5 (95.3, 99.7)
9 months	NE (NE, NE)	95.4 (90.8, 100.0)
12 months	NE (NE, NE)	95.4 (90.8, 100.0)
18 months	NE (NE, NE)	95.4 (90.8, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	0	3 (1.4)
Number of Subjects Censored, n (%)	90 (100.0)	212 (98.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.289

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.5 (96.7, 100.0)
6 months	100.0 (100.0, 100.0)	98.5 (96.7, 100.0)
9 months	NE (NE, NE)	98.5 (96.7, 100.0)
12 months	NE (NE, NE)	98.5 (96.7, 100.0)
18 months	NE (NE, NE)	98.5 (96.7, 100.0)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	1 (1.1)	4 (1.9)
Number of Subjects Censored, n (%)	89 (98.9)	211 (98.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.526 (1.119)
95% CI		(0.170, 13.677)
Log-rank p-value		0.717

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.7, 100.0)	98.0 (96.1, 99.9)
6 months	98.9 (96.7, 100.0)	98.0 (96.1, 99.9)
9 months	NE (NE, NE)	98.0 (96.1, 99.9)
12 months	NE (NE, NE)	98.0 (96.1, 99.9)
18 months	NE (NE, NE)	98.0 (96.1, 99.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	2 (2.2)	7 (3.3)
Number of Subjects Censored, n (%)	88 (97.8)	208 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.400 (0.825)
95% CI		(0.278, 7.049)
Log-rank p-value		0.665

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (94.6, 100.0)	96.5 (94.0, 99.1)
6 months	97.7 (94.6, 100.0)	96.5 (94.0, 99.1)
9 months	NE (NE, NE)	96.5 (94.0, 99.1)
12 months	NE (NE, NE)	96.5 (94.0, 99.1)
18 months	NE (NE, NE)	96.5 (94.0, 99.1)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	0	4 (1.9)
Number of Subjects Censored, n (%)	90 (100.0)	211 (98.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.296

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.5 (98.6, 100.0)
6 months	100.0 (100.0, 100.0)	96.6 (93.2, 100.0)
9 months	NE (NE, NE)	96.6 (93.2, 100.0)
12 months	NE (NE, NE)	96.6 (93.2, 100.0)
18 months	NE (NE, NE)	96.6 (93.2, 100.0)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	22 (24.4)	88 (40.9)
Number of Subjects Censored, n (%)	68 (75.6)	127 (59.1)
Time to first TEAE (months)		
25% percentile (95% CI)	1.84 (0.92, NE)	1.58 (0.95, 1.84)
Median (95% CI)	NE (NE, NE)	7.85 (5.55, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.566 (0.241)
95% CI		(0.976, 2.514)
Log-rank p-value		0.069

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	74.9 (65.7, 84.0)	62.7 (56.0, 69.4)
6 months	74.9 (65.7, 84.0)	56.3 (48.6, 64.1)
9 months	NE (NE, NE)	48.3 (38.9, 57.8)
12 months	NE (NE, NE)	48.3 (38.9, 57.8)
18 months	NE (NE, NE)	48.3 (38.9, 57.8)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	5 (5.6)	24 (11.2)
Number of Subjects Censored, n (%)	85 (94.4)	191 (88.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.884 (0.497)
95% CI		(0.711, 4.989)
Log-rank p-value		0.180

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.3 (87.5, 99.1)	89.9 (85.7, 94.0)
6 months	93.3 (87.5, 99.1)	87.8 (82.8, 92.7)
9 months	NE (NE, NE)	85.5 (79.0, 92.0)
12 months	NE (NE, NE)	85.5 (79.0, 92.0)
18 months	NE (NE, NE)	85.5 (79.0, 92.0)
Median Follow-up Time (months)	2.83	3.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	3 (3.3)	24 (11.2)
Number of Subjects Censored, n (%)	87 (96.7)	191 (88.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.773 (0.617)
95% CI		(0.827, 9.301)
Log-rank p-value		0.071

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.6 (92.9, 100.0)	88.8 (84.4, 93.3)
6 months	96.6 (92.9, 100.0)	87.6 (82.6, 92.6)
9 months	NE (NE, NE)	86.0 (80.2, 91.8)
12 months	NE (NE, NE)	86.0 (80.2, 91.8)
18 months	NE (NE, NE)	86.0 (80.2, 91.8)
Median Follow-up Time (months)	2.83	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	4 (4.4)	24 (11.2)
Number of Subjects Censored, n (%)	86 (95.6)	191 (88.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.161 (0.544)
95% CI		(0.744, 6.278)
Log-rank p-value		0.129

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (91.1, 99.8)	89.5 (85.2, 93.8)
6 months	95.5 (91.1, 99.8)	87.2 (82.0, 92.4)
9 months	NE (NE, NE)	85.6 (79.6, 91.6)
12 months	NE (NE, NE)	85.6 (79.6, 91.6)
18 months	NE (NE, NE)	85.6 (79.6, 91.6)
Median Follow-up Time (months)	2.83	3.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	3 (3.3)	8 (3.7)
Number of Subjects Censored, n (%)	87 (96.7)	207 (96.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.836 (0.693)
95% CI		(0.215, 3.250)
Log-rank p-value		0.870

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.6 (92.8, 100.0)	97.0 (94.7, 99.4)
6 months	96.6 (92.8, 100.0)	96.0 (93.0, 99.1)
9 months	NE (NE, NE)	94.3 (89.8, 98.8)
12 months	NE (NE, NE)	94.3 (89.8, 98.8)
18 months	NE (NE, NE)	94.3 (89.8, 98.8)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	2 (2.2)	11 (5.1)
Number of Subjects Censored, n (%)	88 (97.8)	204 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 6.8*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.638 (0.783)
95% CI		(0.353, 7.598)
Log-rank p-value		0.627

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.6, 100.0)	95.6 (92.8, 98.4)
6 months	94.4 (85.5, 100.0)	94.2 (90.4, 98.1)
9 months	NE (NE, NE)	90.7 (83.1, 98.4)
12 months	NE (NE, NE)	90.7 (83.1, 98.4)
18 months	NE (NE, NE)	90.7 (83.1, 98.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	5 (5.6)	9 (4.2)
Number of Subjects Censored, n (%)	85 (94.4)	206 (95.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 6.8*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.659 (0.568)
95% CI		(0.216, 2.005)
Log-rank p-value		0.546

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.5 (87.9, 99.1)	96.6 (94.1, 99.1)
6 months	93.5 (87.9, 99.1)	94.6 (90.9, 98.3)
9 months	NE (NE, NE)	94.6 (90.9, 98.3)
12 months	NE (NE, NE)	94.6 (90.9, 98.3)
18 months	NE (NE, NE)	94.6 (90.9, 98.3)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	1 (1.1)	13 (6.0)
Number of Subjects Censored, n (%)	89 (98.9)	202 (94.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.375 (1.040)
95% CI		(0.700, 41.289)
Log-rank p-value		0.067

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.7, 100.0)	93.7 (90.3, 97.0)
6 months	98.9 (96.7, 100.0)	93.7 (90.3, 97.0)
9 months	NE (NE, NE)	93.7 (90.3, 97.0)
12 months	NE (NE, NE)	93.7 (90.3, 97.0)
18 months	NE (NE, NE)	93.7 (90.3, 97.0)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	1 (1.1)	11 (5.1)
Number of Subjects Censored, n (%)	89 (98.9)	204 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.710 (1.050)
95% CI		(0.474, 29.048)
Log-rank p-value		0.208

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.7, 100.0)	95.3 (92.4, 98.3)
6 months	98.9 (96.7, 100.0)	94.1 (90.3, 97.9)
9 months	NE (NE, NE)	92.7 (88.1, 97.4)
12 months	NE (NE, NE)	92.7 (88.1, 97.4)
18 months	NE (NE, NE)	92.7 (88.1, 97.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	1 (1.1)	6 (2.8)
Number of Subjects Censored, n (%)	89 (98.9)	209 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.842 (1.099)
95% CI		(0.214, 15.877)
Log-rank p-value		0.601

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.6, 100.0)	97.2 (94.7, 99.7)
6 months	98.9 (96.6, 100.0)	97.2 (94.7, 99.7)
9 months	NE (NE, NE)	95.4 (91.1, 99.7)
12 months	NE (NE, NE)	95.4 (91.1, 99.7)
18 months	NE (NE, NE)	95.4 (91.1, 99.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	1 (1.1)	4 (1.9)
Number of Subjects Censored, n (%)	89 (98.9)	211 (98.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.164 (1.158)
95% CI		(0.120, 11.261)
Log-rank p-value		0.896

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.6, 100.0)	98.4 (96.6, 100.0)
6 months	98.9 (96.6, 100.0)	98.4 (96.6, 100.0)
9 months	NE (NE, NE)	96.6 (92.5, 100.0)
12 months	NE (NE, NE)	96.6 (92.5, 100.0)
18 months	NE (NE, NE)	96.6 (92.5, 100.0)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	20 (22.2)	69 (32.1)
Number of Subjects Censored, n (%)	70 (77.8)	146 (67.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	1.77 (0.99, 3.81)
Median (95% CI)	NE (NE, NE)	NE (9.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.307 (0.257)
95% CI		(0.791, 2.161)
Log-rank p-value		0.323

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.7 (67.6, 85.7)	69.9 (63.7, 76.1)
6 months	76.7 (67.6, 85.7)	65.8 (58.7, 72.9)
9 months	NE (NE, NE)	64.4 (57.0, 71.9)
12 months	NE (NE, NE)	59.5 (47.9, 71.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.22	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	3 (3.3)	26 (12.1)
Number of Subjects Censored, n (%)	87 (96.7)	189 (87.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.427 (0.611)
95% CI		(1.035, 11.354)
Log-rank p-value		0.028

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.5 (92.7, 100.0)	88.1 (83.7, 92.5)
6 months	96.5 (92.7, 100.0)	87.3 (82.6, 91.9)
9 months	NE (NE, NE)	87.3 (82.6, 91.9)
12 months	NE (NE, NE)	87.3 (82.6, 91.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	7 (7.8)	19 (8.8)
Number of Subjects Censored, n (%)	83 (92.2)	196 (91.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.005 (0.445)
95% CI		(0.420, 2.405)
Log-rank p-value		0.941

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.7 (85.8, 97.7)	91.7 (87.9, 95.5)
6 months	91.7 (85.8, 97.7)	89.5 (84.8, 94.3)
9 months	NE (NE, NE)	89.5 (84.8, 94.3)
12 months	NE (NE, NE)	89.5 (84.8, 94.3)
18 months	NE (NE, NE)	89.5 (84.8, 94.3)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	9 (10.0)	12 (5.6)
Number of Subjects Censored, n (%)	81 (90.0)	203 (94.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.433 (0.450)
95% CI		(0.179, 1.045)
Log-rank p-value		0.067

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.5 (83.0, 96.0)	95.1 (92.1, 98.1)
6 months	89.5 (83.0, 96.0)	93.2 (89.2, 97.1)
9 months	NE (NE, NE)	93.2 (89.2, 97.1)
12 months	NE (NE, NE)	93.2 (89.2, 97.1)
18 months	NE (NE, NE)	93.2 (89.2, 97.1)
Median Follow-up Time (months)	2.58	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	1 (1.1)	7 (3.3)
Number of Subjects Censored, n (%)	89 (98.9)	208 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.901 (1.084)
95% CI		(0.347, 24.258)
Log-rank p-value		0.304

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.7, 100.0)	96.7 (94.3, 99.1)
6 months	98.9 (96.7, 100.0)	96.7 (94.3, 99.1)
9 months	NE (NE, NE)	96.7 (94.3, 99.1)
12 months	NE (NE, NE)	96.7 (94.3, 99.1)
18 months	NE (NE, NE)	96.7 (94.3, 99.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	0	5 (2.3)
Number of Subjects Censored, n (%)	90 (100.0)	210 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.361

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.1 (97.7, 100.0)
6 months	100.0 (100.0, 100.0)	97.9 (95.3, 100.0)
9 months	NE (NE, NE)	94.4 (89.1, 99.8)
12 months	NE (NE, NE)	94.4 (89.1, 99.8)
18 months	NE (NE, NE)	94.4 (89.1, 99.8)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Vascular disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	15 (16.7)	95 (44.2)
Number of Subjects Censored, n (%)	75 (83.3)	120 (55.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.81, NE)	0.69 (0.56, 0.99)
Median (95% CI)	NE (NE, NE)	NE (2.86, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.110 (0.279)
95% CI		(1.799, 5.376)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Vascular disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.4 (74.3, 90.5)	56.7 (49.9, 63.5)
6 months	82.4 (74.3, 90.5)	51.3 (43.7, 59.0)
9 months	NE (NE, NE)	51.3 (43.7, 59.0)
12 months	NE (NE, NE)	51.3 (43.7, 59.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	2.07

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	9 (10.0)	90 (41.9)
Number of Subjects Censored, n (%)	81 (90.0)	125 (58.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.69 (0.69, 1.02)
Median (95% CI)	NE (NE, NE)	NE (4.47, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.904 (0.351)
95% CI		(2.464, 9.761)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.4 (82.9, 96.0)	59.4 (52.6, 66.1)
6 months	89.4 (82.9, 96.0)	55.1 (47.6, 62.5)
9 months	NE (NE, NE)	53.0 (44.7, 61.2)
12 months	NE (NE, NE)	53.0 (44.7, 61.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.74	2.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	18 (20.0)	77 (35.8)
Number of Subjects Censored, n (%)	72 (80.0)	138 (64.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.61, NE)	1.38 (0.92, 2.00)
Median (95% CI)	NE (NE, NE)	NE (7.20, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.863 (0.271)
95% CI		(1.095, 3.171)
Log-rank p-value		0.026

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.9 (68.7, 87.1)	66.1 (59.6, 72.7)
6 months	77.9 (68.7, 87.1)	61.6 (54.1, 69.0)
9 months	NE (NE, NE)	55.9 (46.7, 65.1)
12 months	NE (NE, NE)	55.9 (46.7, 65.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	6 (6.7)	24 (11.2)
Number of Subjects Censored, n (%)	84 (93.3)	191 (88.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 8.4*	0.4, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.742 (0.499)
95% CI		(0.656, 4.627)
Log-rank p-value		0.286

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.0 (87.5, 98.4)	89.8 (85.5, 94.1)
6 months	93.0 (87.5, 98.4)	86.2 (80.8, 91.6)
9 months	NE (NE, NE)	86.2 (80.8, 91.6)
12 months	NE (NE, NE)	86.2 (80.8, 91.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.52

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	3 (3.3)	29 (13.5)
Number of Subjects Censored, n (%)	87 (96.7)	186 (86.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.20, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.164 (0.615)
95% CI		(0.949, 10.552)
Log-rank p-value		0.058

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.5 (92.6, 100.0)	88.9 (84.6, 93.2)
6 months	96.5 (92.6, 100.0)	85.7 (80.1, 91.2)
9 months	NE (NE, NE)	79.3 (70.5, 88.0)
12 months	NE (NE, NE)	79.3 (70.5, 88.0)
18 months	NE (NE, NE)	79.3 (70.5, 88.0)
Median Follow-up Time (months)	2.83	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	0	10 (4.7)
Number of Subjects Censored, n (%)	90 (100.0)	205 (95.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.037

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.7 (93.0, 98.5)
6 months	100.0 (100.0, 100.0)	94.6 (91.0, 98.1)
9 months	NE (NE, NE)	94.6 (91.0, 98.1)
12 months	NE (NE, NE)	94.6 (91.0, 98.1)
18 months	NE (NE, NE)	94.6 (91.0, 98.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	4 (4.4)	7 (3.3)
Number of Subjects Censored, n (%)	86 (95.6)	208 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.627 (0.640)
95% CI		(0.179, 2.200)
Log-rank p-value		0.487

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (91.0, 99.8)	97.2 (94.9, 99.4)
6 months	95.4 (91.0, 99.8)	95.8 (92.4, 99.2)
9 months	NE (NE, NE)	95.8 (92.4, 99.2)
12 months	NE (NE, NE)	95.8 (92.4, 99.2)
18 months	NE (NE, NE)	95.8 (92.4, 99.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	1 (1.1)	9 (4.2)
Number of Subjects Censored, n (%)	89 (98.9)	206 (95.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.437 (1.057)
95% CI		(0.433, 27.275)
Log-rank p-value		0.227

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.7, 100.0)	96.2 (93.5, 98.8)
6 months	98.9 (96.7, 100.0)	94.9 (91.4, 98.5)
9 months	NE (NE, NE)	94.9 (91.4, 98.5)
12 months	NE (NE, NE)	94.9 (91.4, 98.5)
18 months	NE (NE, NE)	94.9 (91.4, 98.5)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	0	7 (3.3)
Number of Subjects Censored, n (%)	90 (100.0)	208 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.101

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.7 (94.2, 99.1)
6 months	100.0 (100.0, 100.0)	96.7 (94.2, 99.1)
9 months	NE (NE, NE)	96.7 (94.2, 99.1)
12 months	NE (NE, NE)	96.7 (94.2, 99.1)
18 months	NE (NE, NE)	96.7 (94.2, 99.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	14 (15.6)	73 (34.0)
Number of Subjects Censored, n (%)	76 (84.4)	142 (66.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	1.58 (0.69, 2.56)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.404 (0.303)
95% CI		(1.326, 4.357)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.1 (77.6, 92.6)	67.9 (61.6, 74.3)
6 months	80.4 (68.9, 91.8)	63.9 (56.7, 71.1)
9 months	NE (NE, NE)	59.7 (50.9, 68.5)
12 months	NE (NE, NE)	59.7 (50.9, 68.5)
18 months	NE (NE, NE)	59.7 (50.9, 68.5)
Median Follow-up Time (months)	2.71	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	3 (3.3)	47 (21.9)
Number of Subjects Censored, n (%)	87 (96.7)	168 (78.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	7.39 (2.30, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		9.542 (0.724)
95% CI		(2.309, 39.435)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.6 (92.7, 100.0)	79.9 (74.4, 85.3)
6 months	96.6 (92.7, 100.0)	75.5 (68.9, 82.2)
9 months	NE (NE, NE)	73.2 (65.3, 81.1)
12 months	NE (NE, NE)	73.2 (65.3, 81.1)
18 months	NE (NE, NE)	73.2 (65.3, 81.1)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	3 (3.3)	9 (4.2)
Number of Subjects Censored, n (%)	87 (96.7)	206 (95.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.176 (0.669)
95% CI		(0.317, 4.368)
Log-rank p-value		0.838

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.6 (92.9, 100.0)	95.7 (93.0, 98.5)
6 months	96.6 (92.9, 100.0)	95.7 (93.0, 98.5)
9 months	NE (NE, NE)	95.7 (93.0, 98.5)
12 months	NE (NE, NE)	95.7 (93.0, 98.5)
18 months	NE (NE, NE)	95.7 (93.0, 98.5)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	2 (2.2)	5 (2.3)
Number of Subjects Censored, n (%)	88 (97.8)	210 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.649 (0.862)
95% CI		(0.120, 3.516)
Log-rank p-value		0.597

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.6, 100.0)	97.9 (95.9, 99.9)
6 months	94.4 (85.5, 100.0)	97.1 (94.4, 99.7)
9 months	NE (NE, NE)	97.1 (94.4, 99.7)
12 months	NE (NE, NE)	97.1 (94.4, 99.7)
18 months	NE (NE, NE)	97.1 (94.4, 99.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Nervous system disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	18 (20.0)	64 (29.8)
Number of Subjects Censored, n (%)	72 (80.0)	151 (70.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.45, NE)	2.40 (1.35, 5.49)
Median (95% CI)	NE (NE, NE)	NE (11.10, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.293 (0.272)
95% CI		(0.759, 2.202)
Log-rank p-value		0.448

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Nervous system disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.5 (69.5, 87.4)	72.8 (66.6, 78.9)
6 months	78.5 (69.5, 87.4)	66.6 (59.1, 74.0)
9 months	NE (NE, NE)	65.2 (57.5, 72.9)
12 months	NE (NE, NE)	58.7 (44.7, 72.7)
18 months	NE (NE, NE)	58.7 (44.7, 72.7)
Median Follow-up Time (months)	2.51	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	7 (7.8)	25 (11.6)
Number of Subjects Censored, n (%)	83 (92.2)	190 (88.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.474 (0.432)
95% CI		(0.632, 3.440)
Log-rank p-value		0.384

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (85.1, 97.6)	89.1 (84.9, 93.3)
6 months	91.3 (85.1, 97.6)	88.1 (83.5, 92.7)
9 months	NE (NE, NE)	86.7 (81.4, 92.0)
12 months	NE (NE, NE)	86.7 (81.4, 92.0)
18 months	NE (NE, NE)	86.7 (81.4, 92.0)
Median Follow-up Time (months)	2.83	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	2 (2.2)	3 (1.4)
Number of Subjects Censored, n (%)	88 (97.8)	212 (98.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.645 (0.924)
95% CI		(0.106, 3.946)
Log-rank p-value		0.464

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (94.7, 100.0)	98.5 (96.8, 100.0)
6 months	97.8 (94.7, 100.0)	98.5 (96.8, 100.0)
9 months	NE (NE, NE)	98.5 (96.8, 100.0)
12 months	NE (NE, NE)	98.5 (96.8, 100.0)
18 months	NE (NE, NE)	98.5 (96.8, 100.0)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	2 (2.2)	7 (3.3)
Number of Subjects Censored, n (%)	88 (97.8)	208 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.276 (0.805)
95% CI		(0.264, 6.180)
Log-rank p-value		0.841

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (94.4, 100.0)	96.6 (94.1, 99.1)
6 months	97.6 (94.4, 100.0)	96.6 (94.1, 99.1)
9 months	NE (NE, NE)	96.6 (94.1, 99.1)
12 months	NE (NE, NE)	96.6 (94.1, 99.1)
18 months	NE (NE, NE)	96.6 (94.1, 99.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	9 (10.0)	55 (25.6)
Number of Subjects Censored, n (%)	81 (90.0)	160 (74.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	4.57 (2.46, NE)
Median (95% CI)	NE (NE, NE)	11.96 (11.96, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (11.96, NE)
Min, Max	0.0, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.428 (0.363)
95% CI		(1.192, 4.945)
Log-rank p-value		0.013

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.5 (84.2, 96.8)	77.2 (71.3, 83.0)
6 months	85.7 (74.9, 96.6)	69.7 (62.1, 77.2)
9 months	NE (NE, NE)	67.8 (59.7, 76.0)
12 months	NE (NE, NE)	45.2 (8.6, 81.8)
18 months	NE (NE, NE)	45.2 (8.6, 81.8)
Median Follow-up Time (months)	2.74	2.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	4 (4.4)	40 (18.6)
Number of Subjects Censored, n (%)	86 (95.6)	175 (81.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.75, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.104 (0.528)
95% CI		(1.459, 11.541)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.2 (90.5, 99.8)	82.3 (76.8, 87.7)
6 months	95.2 (90.5, 99.8)	78.4 (72.0, 84.8)
9 months	NE (NE, NE)	75.4 (66.9, 83.8)
12 months	NE (NE, NE)	75.4 (66.9, 83.8)
18 months	NE (NE, NE)	75.4 (66.9, 83.8)
Median Follow-up Time (months)	2.83	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	2 (2.2)	4 (1.9)
Number of Subjects Censored, n (%)	88 (97.8)	211 (98.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.841 (0.866)
95% CI		(0.154, 4.595)
Log-rank p-value		0.846

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (94.6, 100.0)	98.1 (96.3, 99.9)
6 months	97.7 (94.6, 100.0)	98.1 (96.3, 99.9)
9 months	NE (NE, NE)	98.1 (96.3, 99.9)
12 months	NE (NE, NE)	98.1 (96.3, 99.9)
18 months	NE (NE, NE)	98.1 (96.3, 99.9)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Infections and infestations**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	14 (15.6)	50 (23.3)
Number of Subjects Censored, n (%)	76 (84.4)	165 (76.7)
Time to first TEAE (months)		
25% percentile (95% CI)	5.78 (3.71, NE)	6.28 (3.71, 7.69)
Median (95% CI)	NE (5.78, NE)	17.48 (8.21, NE)
75% percentile (95% CI)	NE (NE, NE)	17.48 (NE, NE)
Min, Max	0.0, 6.8*	0.1, 17.5
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.182 (0.322)
95% CI		(0.629, 2.220)
Log-rank p-value		0.547

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Infections and infestations**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.7 (78.1, 93.3)	82.4 (77.1, 87.6)
6 months	67.5 (41.5, 93.4)	75.4 (68.0, 82.7)
9 months	NE (NE, NE)	60.0 (47.9, 72.0)
12 months	NE (NE, NE)	60.0 (47.9, 72.0)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.78	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	4 (4.4)	14 (6.5)
Number of Subjects Censored, n (%)	86 (95.6)	201 (93.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.120 (0.588)
95% CI		(0.354, 3.545)
Log-rank p-value		0.807

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (94.6, 100.0)	95.1 (92.1, 98.1)
6 months	86.6 (71.5, 100.0)	93.7 (89.7, 97.7)
9 months	NE (NE, NE)	88.5 (81.7, 95.4)
12 months	NE (NE, NE)	88.5 (81.7, 95.4)
18 months	NE (NE, NE)	88.5 (81.7, 95.4)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	2 (2.2)	6 (2.8)
Number of Subjects Censored, n (%)	88 (97.8)	209 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.877 (0.832)
95% CI		(0.172, 4.481)
Log-rank p-value		0.836

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (93.3, 100.0)	97.9 (95.9, 99.9)
6 months	97.2 (93.3, 100.0)	95.9 (92.4, 99.4)
9 months	NE (NE, NE)	95.9 (92.4, 99.4)
12 months	NE (NE, NE)	95.9 (92.4, 99.4)
18 months	NE (NE, NE)	95.9 (92.4, 99.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	0	3 (1.4)
Number of Subjects Censored, n (%)	90 (100.0)	212 (98.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.363

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.0 (97.7, 100.0)
6 months	100.0 (100.0, 100.0)	97.8 (95.0, 100.0)
9 months	NE (NE, NE)	97.8 (95.0, 100.0)
12 months	NE (NE, NE)	97.8 (95.0, 100.0)
18 months	NE (NE, NE)	97.8 (95.0, 100.0)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	13 (14.4)	32 (14.9)
Number of Subjects Censored, n (%)	77 (85.6)	183 (85.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.04, NE)	NE (6.47, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.806 (0.335)
95% CI		(0.418, 1.554)
Log-rank p-value		0.509

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.4 (76.5, 92.2)	87.2 (82.5, 91.8)
6 months	84.4 (76.5, 92.2)	84.1 (78.4, 89.8)
9 months	NE (NE, NE)	79.3 (71.8, 86.8)
12 months	NE (NE, NE)	79.3 (71.8, 86.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.71	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	10 (11.1)	19 (8.8)
Number of Subjects Censored, n (%)	80 (88.9)	196 (91.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 6.8*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.563 (0.403)
95% CI		(0.256, 1.239)
Log-rank p-value		0.158

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.2 (81.3, 95.1)	92.9 (89.3, 96.5)
6 months	88.2 (81.3, 95.1)	89.9 (84.9, 94.8)
9 months	NE (NE, NE)	87.0 (80.8, 93.2)
12 months	NE (NE, NE)	87.0 (80.8, 93.2)
18 months	NE (NE, NE)	87.0 (80.8, 93.2)
Median Follow-up Time (months)	2.74	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	0	11 (5.1)
Number of Subjects Censored, n (%)	90 (100.0)	204 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.6*, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.035

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (91.6, 97.7)
6 months	100.0 (100.0, 100.0)	94.7 (91.6, 97.7)
9 months	NE (NE, NE)	94.7 (91.6, 97.7)
12 months	NE (NE, NE)	94.7 (91.6, 97.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Endocrine disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	1 (1.1)	57 (26.5)
Number of Subjects Censored, n (%)	89 (98.9)	158 (73.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.65 (2.10, 5.98)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.6*, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		21.258 (1.010)
95% CI		(2.935, 153.982)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Endocrine disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.6, 100.0)	76.4 (70.5, 82.3)
6 months	98.9 (96.6, 100.0)	66.4 (58.0, 74.8)
9 months	NE (NE, NE)	63.0 (53.8, 72.3)
12 months	NE (NE, NE)	63.0 (53.8, 72.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	1 (1.1)	54 (25.1)
Number of Subjects Censored, n (%)	89 (98.9)	161 (74.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.07 (2.53, 6.01)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.6*, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		19.727 (1.011)
95% CI		(2.720, 143.071)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.6, 100.0)	77.9 (72.1, 83.7)
6 months	98.9 (96.6, 100.0)	68.0 (59.7, 76.3)
9 months	NE (NE, NE)	64.8 (55.7, 73.8)
12 months	NE (NE, NE)	64.8 (55.7, 73.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	7 (7.8)	24 (11.2)
Number of Subjects Censored, n (%)	83 (92.2)	191 (88.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.124 (0.439)
95% CI		(0.476, 2.654)
Log-rank p-value		0.737

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.7 (85.7, 97.6)	89.2 (84.8, 93.6)
6 months	91.7 (85.7, 97.6)	87.2 (82.1, 92.4)
9 months	NE (NE, NE)	85.6 (79.6, 91.5)
12 months	NE (NE, NE)	85.6 (79.6, 91.5)
18 months	NE (NE, NE)	85.6 (79.6, 91.5)
Median Follow-up Time (months)	2.81	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	6 (6.7)	11 (5.1)
Number of Subjects Censored, n (%)	84 (93.3)	204 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 8.4*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.540 (0.531)
95% CI		(0.191, 1.527)
Log-rank p-value		0.360

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.8 (87.1, 98.4)	95.8 (92.8, 98.7)
6 months	92.8 (87.1, 98.4)	94.1 (90.4, 97.8)
9 months	NE (NE, NE)	92.4 (87.6, 97.3)
12 months	NE (NE, NE)	92.4 (87.6, 97.3)
18 months	NE (NE, NE)	92.4 (87.6, 97.3)
Median Follow-up Time (months)	2.81	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	1 (1.1)	6 (2.8)
Number of Subjects Censored, n (%)	89 (98.9)	209 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.074 (1.096)
95% CI		(0.242, 17.760)
Log-rank p-value		0.515

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.4, 100.0)	97.3 (94.9, 99.7)
6 months	98.8 (96.4, 100.0)	96.1 (92.8, 99.4)
9 months	NE (NE, NE)	96.1 (92.8, 99.4)
12 months	NE (NE, NE)	96.1 (92.8, 99.4)
18 months	NE (NE, NE)	96.1 (92.8, 99.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	0	2 (0.9)
Number of Subjects Censored, n (%)	90 (100.0)	213 (99.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.429

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.0 (97.7, 100.0)
6 months	100.0 (100.0, 100.0)	99.0 (97.7, 100.0)
9 months	NE (NE, NE)	99.0 (97.7, 100.0)
12 months	NE (NE, NE)	99.0 (97.7, 100.0)
18 months	NE (NE, NE)	99.0 (97.7, 100.0)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	11 (12.2)	16 (7.4)
Number of Subjects Censored, n (%)	79 (87.8)	199 (92.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.399 (0.408)
95% CI		(0.180, 0.889)
Log-rank p-value		0.024

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.1 (80.0, 94.2)	94.3 (91.1, 97.6)
6 months	87.1 (80.0, 94.2)	89.1 (83.6, 94.6)
9 months	NE (NE, NE)	89.1 (83.6, 94.6)
12 months	NE (NE, NE)	89.1 (83.6, 94.6)
18 months	NE (NE, NE)	89.1 (83.6, 94.6)
Median Follow-up Time (months)	2.81	3.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	3 (3.3)	5 (2.3)
Number of Subjects Censored, n (%)	87 (96.7)	210 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6*, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.479 (0.743)
95% CI		(0.112, 2.056)
Log-rank p-value		0.295

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.3 (92.1, 100.0)	97.8 (95.7, 99.9)
6 months	96.3 (92.1, 100.0)	96.9 (94.2, 99.7)
9 months	NE (NE, NE)	96.9 (94.2, 99.7)
12 months	NE (NE, NE)	96.9 (94.2, 99.7)
18 months	NE (NE, NE)	96.9 (94.2, 99.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3C
Summary of Time to Onset of TEAE by SOC/PT by Sex
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Female

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Number of Subjects with Events, n (%)	1 (1.1)	5 (2.3)
Number of Subjects Censored, n (%)	89 (98.9)	210 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.280 (1.130)
95% CI		(0.140, 11.719)
Log-rank p-value		0.707

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
North America

Statistics	Placebo + BSC N=90	Fruquintinib + BSC N=215
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.7, 100.0)	98.0 (96.1, 99.9)
6 months	98.9 (96.7, 100.0)	96.8 (93.6, 99.9)
9 months	NE (NE, NE)	96.8 (93.6, 99.9)
12 months	NE (NE, NE)	96.8 (93.6, 99.9)
18 months	NE (NE, NE)	96.8 (93.6, 99.9)
Median Follow-up Time (months)	2.83	3.75

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	22 (53.7)	54 (67.5)
Number of Subjects Censored, n (%)	19 (46.3)	26 (32.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.33, 1.22)	0.43 (0.23, 0.69)
Median (95% CI)	2.56 (0.95, NE)	1.25 (0.69, 2.07)
75% percentile (95% CI)	NE (3.71, NE)	6.97 (3.32, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Min, Max	0.0, 4.9*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.322 (0.259)
95% CI		(0.796, 2.196)
Log-rank p-value		0.347

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	46.8 (30.9, 62.8)	35.8 (24.9, 46.7)
6 months	NE (NE, NE)	28.8 (17.4, 40.3)
9 months	NE (NE, NE)	23.1 (9.4, 36.7)
12 months	NE (NE, NE)	23.1 (9.4, 36.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.64	1.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	1 (2.4)	0
Number of Subjects Censored, n (%)	40 (97.6)	80 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.8*, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.075

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (91.9, 100.0)	100.0 (100.0, 100.0)
6 months	97.2 (91.9, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	13 (31.7)	43 (53.8)
Number of Subjects Censored, n (%)	28 (68.3)	37 (46.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.62, NE)	0.69 (0.39, 1.12)
Median (95% CI)	NE (NE, NE)	2.73 (1.38, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (6.97, NE)
Min, Max	0.0, 5.6*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.744 (0.321)
95% CI		(0.930, 3.270)
Log-rank p-value		0.108

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	67.7 (53.1, 82.2)	47.3 (35.8, 58.8)
6 months	NE (NE, NE)	43.2 (31.4, 55.1)
9 months	NE (NE, NE)	37.0 (21.9, 52.2)
12 months	NE (NE, NE)	37.0 (21.9, 52.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	1.64

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	6 (14.6)	8 (10.0)
Number of Subjects Censored, n (%)	35 (85.4)	72 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.35, NE)	NE (6.11, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 8.4*	0.1, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.557 (0.573)
95% CI		(0.181, 1.712)
Log-rank p-value		0.386

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.6 (73.2, 96.0)	92.0 (85.8, 98.2)
6 months	84.6 (73.2, 96.0)	89.8 (82.4, 97.2)
9 months	NE (NE, NE)	85.7 (75.2, 96.3)
12 months	NE (NE, NE)	85.7 (75.2, 96.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	4 (5.0)
Number of Subjects Censored, n (%)	41 (100.0)	76 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.2, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.112

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.5 (89.2, 99.8)
6 months	100.0 (100.0, 100.0)	94.5 (89.2, 99.8)
9 months	NE (NE, NE)	94.5 (89.2, 99.8)
12 months	NE (NE, NE)	94.5 (89.2, 99.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	4 (9.8)	3 (3.8)
Number of Subjects Censored, n (%)	37 (90.2)	77 (96.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.94, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.8*, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.230 (0.782)
95% CI		(0.050, 1.065)
Log-rank p-value		0.095

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.2 (79.2, 99.3)	98.7 (96.3, 100.0)
6 months	89.2 (79.2, 99.3)	94.5 (88.2, 100.0)
9 months	NE (NE, NE)	94.5 (88.2, 100.0)
12 months	NE (NE, NE)	94.5 (88.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	7 (17.1)	5 (6.3)
Number of Subjects Censored, n (%)	34 (82.9)	75 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.99, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.2, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.282 (0.595)
95% CI		(0.088, 0.907)
Log-rank p-value		0.023

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.8 (67.5, 94.1)	93.6 (88.2, 99.0)
6 months	80.8 (67.5, 94.1)	93.6 (88.2, 99.0)
9 months	NE (NE, NE)	93.6 (88.2, 99.0)
12 months	NE (NE, NE)	93.6 (88.2, 99.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	1 (2.4)	6 (7.5)
Number of Subjects Censored, n (%)	40 (97.6)	74 (92.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.98, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 8.4*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.725 (1.109)
95% CI		(0.310, 23.937)
Log-rank p-value		0.335

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (92.8, 100.0)	94.9 (90.0, 99.8)
6 months	97.6 (92.8, 100.0)	88.4 (78.2, 98.6)
9 months	NE (NE, NE)	88.4 (78.2, 98.6)
12 months	NE (NE, NE)	88.4 (78.2, 98.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	25 (61.0)	64 (80.0)
Number of Subjects Censored, n (%)	16 (39.0)	16 (20.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.59 (0.07, 0.72)	0.39 (0.23, 0.62)
Median (95% CI)	1.38 (0.69, NE)	0.97 (0.69, 1.45)
75% percentile (95% CI)	NE (1.71, NE)	2.56 (1.58, 5.19)
Min, Max	0.0, 4.6*	0.0, 7.7*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.287 (0.242)
95% CI		(0.801, 2.070)
Log-rank p-value		0.312

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	34.1 (17.7, 50.4)	22.6 (13.0, 32.2)
6 months	NE (NE, NE)	6.9 (0.0, 17.6)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.22	0.97

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	8 (19.5)	21 (26.3)
Number of Subjects Censored, n (%)	33 (80.5)	59 (73.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	5.78 (1.68, 7.33)
Median (95% CI)	NE (NE, NE)	NE (6.70, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.0, 9.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.020 (0.437)
95% CI		(0.433, 2.405)
Log-rank p-value		0.940

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.4 (66.5, 92.2)	78.4 (69.0, 87.9)
6 months	NE (NE, NE)	68.2 (54.4, 82.1)
9 months	NE (NE, NE)	55.1 (34.9, 75.3)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	14 (34.1)	28 (35.0)
Number of Subjects Censored, n (%)	27 (65.9)	52 (65.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.92 (0.59, NE)	1.58 (0.72, 3.35)
Median (95% CI)	NE (1.61, NE)	NE (4.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.751 (0.340)
95% CI		(0.386, 1.461)
Log-rank p-value		0.371

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	65.1 (50.2, 79.9)	66.0 (54.9, 77.1)
6 months	65.1 (50.2, 79.9)	58.7 (46.1, 71.3)
9 months	NE (NE, NE)	58.7 (46.1, 71.3)
12 months	NE (NE, NE)	58.7 (46.1, 71.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	11 (26.8)	23 (28.8)
Number of Subjects Censored, n (%)	30 (73.2)	57 (71.3)
Time to first TEAE (months)		
25% percentile (95% CI)	1.91 (0.69, NE)	2.99 (1.91, 5.19)
Median (95% CI)	NE (4.57, NE)	NE (5.19, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 4.9*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.699 (0.382)
95% CI		(0.330, 1.480)
Log-rank p-value		0.564

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.5 (59.3, 87.7)	73.6 (62.9, 84.4)
6 months	NE (NE, NE)	62.7 (49.1, 76.2)
9 months	NE (NE, NE)	59.0 (44.4, 73.5)
12 months	NE (NE, NE)	59.0 (44.4, 73.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	9 (22.0)	19 (23.8)
Number of Subjects Censored, n (%)	32 (78.0)	61 (76.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	2.89 (2.27, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.2, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.853 (0.413)
95% CI		(0.380, 1.916)
Log-rank p-value		0.949

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.5 (64.5, 90.5)	74.2 (63.7, 84.7)
6 months	77.5 (64.5, 90.5)	70.8 (58.9, 82.7)
9 months	NE (NE, NE)	70.8 (58.9, 82.7)
12 months	NE (NE, NE)	70.8 (58.9, 82.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	8 (19.5)	22 (27.5)
Number of Subjects Censored, n (%)	33 (80.5)	58 (72.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	3.35 (1.54, NE)
Median (95% CI)	NE (NE, NE)	NE (5.82, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.127 (0.424)
95% CI		(0.491, 2.586)
Log-rank p-value		0.764

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.3 (66.4, 92.2)	79.1 (69.9, 88.2)
6 months	79.3 (66.4, 92.2)	62.8 (48.7, 76.9)
9 months	NE (NE, NE)	62.8 (48.7, 76.9)
12 months	NE (NE, NE)	62.8 (48.7, 76.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	2.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	1 (2.4)	17 (21.3)
Number of Subjects Censored, n (%)	40 (97.6)	63 (78.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.58, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.2, 12.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		10.711 (1.035)
95% CI		(1.409, 81.440)
Log-rank p-value		0.008

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (91.6, 100.0)	80.4 (71.5, 89.4)
6 months	97.1 (91.6, 100.0)	75.3 (64.4, 86.2)
9 months	NE (NE, NE)	75.3 (64.4, 86.2)
12 months	NE (NE, NE)	75.3 (64.4, 86.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	2 (4.9)	2 (2.5)
Number of Subjects Censored, n (%)	39 (95.1)	78 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.6, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.519 (1.020)
95% CI		(0.070, 3.835)
Log-rank p-value		0.569

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.7 (87.5, 100.0)	97.1 (93.0, 100.0)
6 months	94.7 (87.5, 100.0)	97.1 (93.0, 100.0)
9 months	NE (NE, NE)	97.1 (93.0, 100.0)
12 months	NE (NE, NE)	97.1 (93.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	2 (2.5)
Number of Subjects Censored, n (%)	41 (100.0)	78 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.6, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.291

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.5 (94.1, 100.0)
6 months	100.0 (100.0, 100.0)	97.5 (94.1, 100.0)
9 months	NE (NE, NE)	97.5 (94.1, 100.0)
12 months	NE (NE, NE)	97.5 (94.1, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	1 (2.4)	4 (5.0)
Number of Subjects Censored, n (%)	40 (97.6)	76 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.2, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.509 (1.121)
95% CI		(0.168, 13.582)
Log-rank p-value		0.604

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.6 (89.9, 100.0)	94.1 (88.3, 99.8)
6 months	96.6 (89.9, 100.0)	94.1 (88.3, 99.8)
9 months	NE (NE, NE)	94.1 (88.3, 99.8)
12 months	NE (NE, NE)	94.1 (88.3, 99.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	1 (2.4)	2 (2.5)
Number of Subjects Censored, n (%)	40 (97.6)	78 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 8.4*	0.8*, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.491 (1.309)
95% CI		(0.038, 6.387)
Log-rank p-value		0.504

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (92.8, 100.0)	98.6 (95.8, 100.0)
6 months	97.6 (92.8, 100.0)	94.5 (86.1, 100.0)
9 months	NE (NE, NE)	94.5 (86.1, 100.0)
12 months	NE (NE, NE)	94.5 (86.1, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	2 (2.5)
Number of Subjects Censored, n (%)	41 (100.0)	78 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.6, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.286

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.4 (93.8, 100.0)
6 months	100.0 (100.0, 100.0)	97.4 (93.8, 100.0)
9 months	NE (NE, NE)	97.4 (93.8, 100.0)
12 months	NE (NE, NE)	97.4 (93.8, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	16 (39.0)	49 (61.3)
Number of Subjects Censored, n (%)	25 (61.0)	31 (38.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.62, 2.83)	0.69 (NE, NE)
Median (95% CI)	NE (1.35, NE)	1.87 (0.95, 3.35)
75% percentile (95% CI)	NE (NE, NE)	NE (5.68, NE)
Min, Max	0.0, 5.6*	0.2, 12.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.490 (0.295)
95% CI		(0.836, 2.656)
Log-rank p-value		0.200

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	57.3 (40.5, 74.1)	40.2 (29.1, 51.4)
6 months	NE (NE, NE)	33.3 (21.4, 45.1)
9 months	NE (NE, NE)	33.3 (21.4, 45.1)
12 months	NE (NE, NE)	33.3 (21.4, 45.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	1.59

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	6 (14.6)	26 (32.5)
Number of Subjects Censored, n (%)	35 (85.4)	54 (67.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	1.61 (0.69, 6.97)
Median (95% CI)	NE (NE, NE)	NE (6.97, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.2, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.051 (0.459)
95% CI		(0.835, 5.040)
Log-rank p-value		0.093

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.3 (74.4, 96.2)	69.9 (59.5, 80.3)
6 months	85.3 (74.4, 96.2)	64.5 (52.3, 76.6)
9 months	NE (NE, NE)	59.9 (45.6, 74.1)
12 months	NE (NE, NE)	59.9 (45.6, 74.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	1 (2.4)	12 (15.0)
Number of Subjects Censored, n (%)	40 (97.6)	68 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.86, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 8.4*	0.7, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.432 (1.044)
95% CI		(0.572, 34.329)
Log-rank p-value		0.096

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (92.8, 100.0)	85.8 (77.5, 94.1)
6 months	97.6 (92.8, 100.0)	80.9 (70.6, 91.1)
9 months	NE (NE, NE)	80.9 (70.6, 91.1)
12 months	NE (NE, NE)	80.9 (70.6, 91.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	4 (9.8)	13 (16.3)
Number of Subjects Censored, n (%)	37 (90.2)	67 (83.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.07, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 5.6*	0.6, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.389 (0.599)
95% CI		(0.429, 4.493)
Log-rank p-value		0.581

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.2 (81.0, 99.3)	86.1 (78.1, 94.2)
6 months	NE (NE, NE)	76.7 (64.2, 89.2)
9 months	NE (NE, NE)	76.7 (64.2, 89.2)
12 months	NE (NE, NE)	76.7 (64.2, 89.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	3.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	2 (4.9)	5 (6.3)
Number of Subjects Censored, n (%)	39 (95.1)	75 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.7, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.054 (0.843)
95% CI		(0.202, 5.496)
Log-rank p-value		0.989

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.9 (85.6, 100.0)	93.2 (87.5, 99.0)
6 months	NE (NE, NE)	93.2 (87.5, 99.0)
9 months	NE (NE, NE)	93.2 (87.5, 99.0)
12 months	NE (NE, NE)	93.2 (87.5, 99.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	9 (11.3)
Number of Subjects Censored, n (%)	41 (100.0)	71 (88.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.43, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.3, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.034

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	89.2 (82.1, 96.3)
6 months	100.0 (100.0, 100.0)	89.2 (82.1, 96.3)
9 months	NE (NE, NE)	82.3 (67.8, 96.8)
12 months	NE (NE, NE)	82.3 (67.8, 96.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	11 (13.8)
Number of Subjects Censored, n (%)	41 (100.0)	69 (86.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.68, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.7, 12.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.015

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	86.5 (78.7, 94.4)
6 months	100.0 (100.0, 100.0)	82.4 (71.6, 93.3)
9 months	NE (NE, NE)	82.4 (71.6, 93.3)
12 months	NE (NE, NE)	82.4 (71.6, 93.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	3 (7.3)	10 (12.5)
Number of Subjects Censored, n (%)	38 (92.7)	70 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.83, NE)	NE (6.51, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 8.4*	0.6, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.260 (0.670)
95% CI		(0.339, 4.684)
Log-rank p-value		0.723

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.8 (78.1, 100.0)	87.7 (80.1, 95.3)
6 months	89.8 (78.1, 100.0)	87.7 (80.1, 95.3)
9 months	NE (NE, NE)	83.3 (72.2, 94.3)
12 months	NE (NE, NE)	83.3 (72.2, 94.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	1 (2.4)	4 (5.0)
Number of Subjects Censored, n (%)	40 (97.6)	76 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 8.4*	0.7, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.630 (1.124)
95% CI		(0.180, 14.752)
Log-rank p-value		0.666

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (92.8, 100.0)	94.4 (89.0, 99.8)
6 months	97.6 (92.8, 100.0)	94.4 (89.0, 99.8)
9 months	NE (NE, NE)	94.4 (89.0, 99.8)
12 months	NE (NE, NE)	94.4 (89.0, 99.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	8 (10.0)
Number of Subjects Censored, n (%)	41 (100.0)	72 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.7, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.051

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	88.9 (81.6, 96.2)
6 months	100.0 (100.0, 100.0)	88.9 (81.6, 96.2)
9 months	NE (NE, NE)	88.9 (81.6, 96.2)
12 months	NE (NE, NE)	88.9 (81.6, 96.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	6 (7.5)
Number of Subjects Censored, n (%)	41 (100.0)	74 (92.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.63, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.7, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.152

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.4 (90.2, 100.0)
6 months	100.0 (100.0, 100.0)	87.2 (77.0, 97.3)
9 months	NE (NE, NE)	87.2 (77.0, 97.3)
12 months	NE (NE, NE)	87.2 (77.0, 97.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	17 (41.5)	53 (66.3)
Number of Subjects Censored, n (%)	24 (58.5)	27 (33.8)
Time to first TEAE (months)		
25% percentile (95% CI)	1.18 (0.76, 1.94)	0.71 (0.69, 0.95)
Median (95% CI)	3.71 (1.71, NE)	1.61 (1.12, 2.79)
75% percentile (95% CI)	NE (3.71, NE)	5.78 (3.68, NE)
Min, Max	0.0, 4.9*	0.1, 12.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.672 (0.290)
95% CI		(0.947, 2.952)
Log-rank p-value		0.067

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	56.5 (39.6, 73.5)	37.3 (26.2, 48.3)
6 months	NE (NE, NE)	24.5 (11.5, 37.5)
9 months	NE (NE, NE)	12.2 (0.0, 30.4)
12 months	NE (NE, NE)	12.2 (0.0, 30.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	1.59

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	8 (19.5)	23 (28.8)
Number of Subjects Censored, n (%)	33 (80.5)	57 (71.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.35, NE)	1.84 (1.41, 7.85)
Median (95% CI)	NE (NE, NE)	NE (6.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8, 8.4*	0.6, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.246 (0.419)
95% CI		(0.548, 2.834)
Log-rank p-value		0.823

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.2 (62.7, 91.7)	75.0 (65.2, 84.8)
6 months	77.2 (62.7, 91.7)	69.1 (56.9, 81.3)
9 months	NE (NE, NE)	54.7 (33.7, 75.7)
12 months	NE (NE, NE)	54.7 (33.7, 75.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	2.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	2 (4.9)	15 (18.8)
Number of Subjects Censored, n (%)	39 (95.1)	65 (81.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	7.43 (2.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 8.4*	0.1, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.341 (0.775)
95% CI		(0.732, 15.254)
Log-rank p-value		0.120

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (88.5, 100.0)	82.1 (73.2, 91.1)
6 months	95.1 (88.5, 100.0)	78.2 (66.9, 89.6)
9 months	NE (NE, NE)	72.2 (56.8, 87.6)
12 months	NE (NE, NE)	72.2 (56.8, 87.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	2 (4.9)	13 (16.3)
Number of Subjects Censored, n (%)	39 (95.1)	67 (83.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	7.43 (4.63, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.7, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.704 (0.774)
95% CI		(0.593, 12.323)
Log-rank p-value		0.203

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (88.4, 100.0)	86.5 (78.7, 94.3)
6 months	95.1 (88.4, 100.0)	83.6 (74.2, 93.0)
9 months	NE (NE, NE)	72.9 (56.6, 89.2)
12 months	NE (NE, NE)	72.9 (56.6, 89.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	1 (2.4)	9 (11.3)
Number of Subjects Censored, n (%)	40 (97.6)	71 (88.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.63, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.4, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.358 (1.064)
95% CI		(0.542, 35.048)
Log-rank p-value		0.231

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (92.7, 100.0)	89.0 (81.7, 96.3)
6 months	97.5 (92.7, 100.0)	86.0 (76.9, 95.1)
9 months	NE (NE, NE)	86.0 (76.9, 95.1)
12 months	NE (NE, NE)	86.0 (76.9, 95.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	2 (4.9)	9 (11.3)
Number of Subjects Censored, n (%)	39 (95.1)	71 (88.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (4.86, NE)
Median (95% CI)	NE (3.71, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.840 (0.804)
95% CI		(0.381, 8.901)
Log-rank p-value		0.384

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.4 (89.6, 100.0)	89.1 (81.9, 96.2)
6 months	NE (NE, NE)	85.8 (76.4, 95.2)
9 months	NE (NE, NE)	85.8 (76.4, 95.2)
12 months	NE (NE, NE)	85.8 (76.4, 95.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.52

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	4 (9.8)	13 (16.3)
Number of Subjects Censored, n (%)	37 (90.2)	67 (83.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.56, NE)	NE (4.86, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.5, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.263 (0.590)
95% CI		(0.397, 4.014)
Log-rank p-value		0.818

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.6 (75.9, 99.3)	85.4 (77.4, 93.4)
6 months	NE (NE, NE)	78.6 (66.9, 90.4)
9 months	NE (NE, NE)	78.6 (66.9, 90.4)
12 months	NE (NE, NE)	78.6 (66.9, 90.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	1 (2.4)	9 (11.3)
Number of Subjects Censored, n (%)	40 (97.6)	71 (88.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.7, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.254 (1.084)
95% CI		(0.508, 35.634)
Log-rank p-value		0.181

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (92.8, 100.0)	89.4 (82.4, 96.4)
6 months	97.6 (92.8, 100.0)	87.2 (79.2, 95.2)
9 months	NE (NE, NE)	87.2 (79.2, 95.2)
12 months	NE (NE, NE)	87.2 (79.2, 95.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	2 (4.9)	8 (10.0)
Number of Subjects Censored, n (%)	39 (95.1)	72 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.04, NE)	NE (5.32, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.7, 12.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.348 (0.814)
95% CI		(0.273, 6.646)
Log-rank p-value		0.862

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.0 (83.6, 100.0)	91.1 (84.1, 98.0)
6 months	93.0 (83.6, 100.0)	83.7 (72.0, 95.5)
9 months	NE (NE, NE)	83.7 (72.0, 95.5)
12 months	NE (NE, NE)	83.7 (72.0, 95.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	6 (7.5)
Number of Subjects Censored, n (%)	41 (100.0)	74 (92.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.8*, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.091

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	92.8 (86.6, 99.0)
6 months	100.0 (100.0, 100.0)	89.7 (81.2, 98.2)
9 months	NE (NE, NE)	89.7 (81.2, 98.2)
12 months	NE (NE, NE)	89.7 (81.2, 98.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	2 (2.5)
Number of Subjects Censored, n (%)	41 (100.0)	78 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.8*, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.239

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.4 (93.9, 100.0)
6 months	100.0 (100.0, 100.0)	97.4 (93.9, 100.0)
9 months	NE (NE, NE)	97.4 (93.9, 100.0)
12 months	NE (NE, NE)	97.4 (93.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	13 (31.7)	35 (43.8)
Number of Subjects Censored, n (%)	28 (68.3)	45 (56.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.66, NE)	0.69 (0.46, 1.38)
Median (95% CI)	NE (NE, NE)	7.56 (2.73, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.358 (0.330)
95% CI		(0.711, 2.594)
Log-rank p-value		0.441

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	67.9 (53.5, 82.3)	60.8 (50.0, 71.6)
6 months	67.9 (53.5, 82.3)	53.5 (41.0, 65.9)
9 months	NE (NE, NE)	46.8 (30.4, 63.2)
12 months	NE (NE, NE)	46.8 (30.4, 63.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.46

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	2 (4.9)	10 (12.5)
Number of Subjects Censored, n (%)	39 (95.1)	70 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 8.4*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.719 (0.785)
95% CI		(0.584, 12.670)
Log-rank p-value		0.170

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.7 (87.5, 100.0)	88.6 (81.6, 95.6)
6 months	94.7 (87.5, 100.0)	86.5 (78.5, 94.5)
9 months	NE (NE, NE)	86.5 (78.5, 94.5)
12 months	NE (NE, NE)	86.5 (78.5, 94.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	3.52

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	5 (12.2)	15 (18.8)
Number of Subjects Censored, n (%)	36 (87.8)	65 (81.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.64, NE)	10.28 (3.25, NE)
Median (95% CI)	NE (NE, NE)	NE (10.28, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (10.28, NE)
Min, Max	0.3, 8.4*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.143 (0.529)
95% CI		(0.405, 3.224)
Log-rank p-value		0.761

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (77.2, 97.8)	85.4 (77.4, 93.5)
6 months	87.5 (77.2, 97.8)	78.0 (67.0, 89.0)
9 months	NE (NE, NE)	78.0 (67.0, 89.0)
12 months	NE (NE, NE)	58.5 (24.4, 92.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	3.47

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	5 (12.2)	12 (15.0)
Number of Subjects Censored, n (%)	36 (87.8)	68 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (2.86, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.2, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.174 (0.542)
95% CI		(0.406, 3.399)
Log-rank p-value		0.731

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.8 (77.8, 97.8)	84.8 (76.4, 93.3)
6 months	87.8 (77.8, 97.8)	82.6 (73.3, 91.9)
9 months	NE (NE, NE)	82.6 (73.3, 91.9)
12 months	NE (NE, NE)	82.6 (73.3, 91.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	6 (7.5)
Number of Subjects Censored, n (%)	41 (100.0)	74 (92.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.3, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.091

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	92.2 (86.1, 98.2)
6 months	100.0 (100.0, 100.0)	92.2 (86.1, 98.2)
9 months	NE (NE, NE)	92.2 (86.1, 98.2)
12 months	NE (NE, NE)	92.2 (86.1, 98.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.52

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	1 (2.4)	5 (6.3)
Number of Subjects Censored, n (%)	40 (97.6)	75 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.97, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 8.4*	0.2, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.329 (1.120)
95% CI		(0.259, 20.914)
Log-rank p-value		0.491

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (92.8, 100.0)	94.9 (90.1, 99.8)
6 months	97.6 (92.8, 100.0)	94.9 (90.1, 99.8)
9 months	NE (NE, NE)	89.0 (76.8, 100.0)
12 months	NE (NE, NE)	89.0 (76.8, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Vascular disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	8 (19.5)	26 (32.5)
Number of Subjects Censored, n (%)	33 (80.5)	54 (67.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	1.64 (0.69, 5.59)
Median (95% CI)	NE (NE, NE)	NE (5.59, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 8.4*	0.2, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.631 (0.417)
95% CI		(0.721, 3.692)
Log-rank p-value		0.289

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Vascular disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.4 (68.2, 92.6)	69.6 (59.1, 80.2)
6 months	80.4 (68.2, 92.6)	62.9 (49.8, 76.0)
9 months	NE (NE, NE)	58.4 (43.6, 73.3)
12 months	NE (NE, NE)	58.4 (43.6, 73.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	2 (4.9)	22 (27.5)
Number of Subjects Censored, n (%)	39 (95.1)	58 (72.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.87 (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 8.4*	0.2, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		7.223 (0.747)
95% CI		(1.671, 31.217)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (88.5, 100.0)	72.9 (63.0, 82.9)
6 months	95.1 (88.5, 100.0)	72.9 (63.0, 82.9)
9 months	NE (NE, NE)	68.1 (55.0, 81.1)
12 months	NE (NE, NE)	68.1 (55.0, 81.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	9 (22.0)	35 (43.8)
Number of Subjects Censored, n (%)	32 (78.0)	45 (56.3)
Time to first TEAE (months)		
25% percentile (95% CI)	3.71 (0.69, NE)	0.71 (0.46, 1.84)
Median (95% CI)	NE (3.71, NE)	9.76 (2.00, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (9.76, NE)
Min, Max	0.0, 8.4*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.035 (0.378)
95% CI		(0.971, 4.265)
Log-rank p-value		0.017

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.6 (66.9, 92.3)	57.0 (45.7, 68.2)
6 months	66.3 (40.3, 92.3)	54.7 (43.0, 66.3)
9 months	NE (NE, NE)	54.7 (43.0, 66.3)
12 months	NE (NE, NE)	27.3 (0.0, 65.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	2.23

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	2 (4.9)	12 (15.0)
Number of Subjects Censored, n (%)	39 (95.1)	68 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.52, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 8.4*	0.4, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.631 (0.770)
95% CI		(0.582, 11.906)
Log-rank p-value		0.204

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (88.5, 100.0)	86.5 (78.7, 94.4)
6 months	95.1 (88.5, 100.0)	82.1 (72.6, 91.6)
9 months	NE (NE, NE)	82.1 (72.6, 91.6)
12 months	NE (NE, NE)	82.1 (72.6, 91.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	1 (2.4)	14 (17.5)
Number of Subjects Censored, n (%)	40 (97.6)	66 (82.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.79, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.1, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.996 (1.041)
95% CI		(0.909, 53.866)
Log-rank p-value		0.032

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (91.6, 100.0)	84.1 (75.8, 92.4)
6 months	97.1 (91.6, 100.0)	79.5 (69.4, 89.5)
9 months	NE (NE, NE)	79.5 (69.4, 89.5)
12 months	NE (NE, NE)	79.5 (69.4, 89.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	2 (4.9)	6 (7.5)
Number of Subjects Censored, n (%)	39 (95.1)	74 (92.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (3.71, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.2, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.196 (0.822)
95% CI		(0.239, 5.992)
Log-rank p-value		0.701

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (92.8, 100.0)	92.4 (86.6, 98.3)
6 months	83.6 (58.0, 100.0)	92.4 (86.6, 98.3)
9 months	NE (NE, NE)	92.4 (86.6, 98.3)
12 months	NE (NE, NE)	92.4 (86.6, 98.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	2 (4.9)	4 (5.0)
Number of Subjects Censored, n (%)	39 (95.1)	76 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 8.4*	0.1, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.129 (0.876)
95% CI		(0.203, 6.291)
Log-rank p-value		0.842

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.8 (87.7, 100.0)	94.6 (89.4, 99.8)
6 months	94.8 (87.7, 100.0)	94.6 (89.4, 99.8)
9 months	NE (NE, NE)	94.6 (89.4, 99.8)
12 months	NE (NE, NE)	94.6 (89.4, 99.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	2 (2.5)
Number of Subjects Censored, n (%)	41 (100.0)	78 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.70, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.8*, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.537

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.6 (96.0, 100.0)
6 months	100.0 (100.0, 100.0)	98.6 (96.0, 100.0)
9 months	NE (NE, NE)	93.2 (82.4, 100.0)
12 months	NE (NE, NE)	93.2 (82.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	6 (7.5)
Number of Subjects Censored, n (%)	41 (100.0)	74 (92.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.1, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.085

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	92.0 (85.8, 98.2)
6 months	100.0 (100.0, 100.0)	92.0 (85.8, 98.2)
9 months	NE (NE, NE)	92.0 (85.8, 98.2)
12 months	NE (NE, NE)	92.0 (85.8, 98.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	6 (14.6)	25 (31.3)
Number of Subjects Censored, n (%)	35 (85.4)	55 (68.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	1.64 (0.72, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 8.4*	0.1, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.957 (0.460)
95% CI		(0.794, 4.825)
Log-rank p-value		0.127

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.4 (74.5, 96.2)	70.1 (59.8, 80.4)
6 months	85.4 (74.5, 96.2)	65.2 (53.6, 76.8)
9 months	NE (NE, NE)	65.2 (53.6, 76.8)
12 months	NE (NE, NE)	65.2 (53.6, 76.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	2.74

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	11 (13.8)
Number of Subjects Censored, n (%)	41 (100.0)	69 (86.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.19, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.4, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.039

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	88.3 (81.1, 95.5)
6 months	100.0 (100.0, 100.0)	82.0 (70.9, 93.1)
9 months	NE (NE, NE)	82.0 (70.9, 93.1)
12 months	NE (NE, NE)	82.0 (70.9, 93.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	2 (4.9)	4 (5.0)
Number of Subjects Censored, n (%)	39 (95.1)	76 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 8.4*	0.1, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.045 (0.886)
95% CI		(0.184, 5.926)
Log-rank p-value		0.932

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (88.5, 100.0)	94.8 (89.8, 99.8)
6 months	95.1 (88.5, 100.0)	94.8 (89.8, 99.8)
9 months	NE (NE, NE)	94.8 (89.8, 99.8)
12 months	NE (NE, NE)	94.8 (89.8, 99.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	1 (2.4)	4 (5.0)
Number of Subjects Censored, n (%)	40 (97.6)	76 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.1, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.926 (1.143)
95% CI		(0.205, 18.110)
Log-rank p-value		0.581

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (92.8, 100.0)	95.8 (91.1, 100.0)
6 months	97.6 (92.8, 100.0)	93.4 (87.0, 99.9)
9 months	NE (NE, NE)	93.4 (87.0, 99.9)
12 months	NE (NE, NE)	93.4 (87.0, 99.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	9 (22.0)	29 (36.3)
Number of Subjects Censored, n (%)	32 (78.0)	51 (63.8)
Time to first TEAE (months)		
25% percentile (95% CI)	2.56 (1.61, NE)	1.31 (0.59, 4.01)
Median (95% CI)	NE (NE, NE)	NE (5.75, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.529 (0.390)
95% CI		(0.711, 3.285)
Log-rank p-value		0.311

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	74.4 (59.5, 89.3)	65.9 (55.1, 76.7)
6 months	NE (NE, NE)	58.7 (45.0, 72.4)
9 months	NE (NE, NE)	53.8 (38.3, 69.4)
12 months	NE (NE, NE)	53.8 (38.3, 69.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	2.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	4 (9.8)	11 (13.8)
Number of Subjects Censored, n (%)	37 (90.2)	69 (86.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.64, NE)	NE (6.11, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 8.4*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.263 (0.595)
95% CI		(0.393, 4.054)
Log-rank p-value		0.674

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.8 (80.3, 99.3)	87.1 (79.6, 94.6)
6 months	89.8 (80.3, 99.3)	87.1 (79.6, 94.6)
9 months	NE (NE, NE)	82.2 (70.6, 93.9)
12 months	NE (NE, NE)	82.2 (70.6, 93.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	2.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	4 (5.0)
Number of Subjects Censored, n (%)	41 (100.0)	76 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.4, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.190

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.5 (89.3, 99.8)
6 months	100.0 (100.0, 100.0)	94.5 (89.3, 99.8)
9 months	NE (NE, NE)	94.5 (89.3, 99.8)
12 months	NE (NE, NE)	94.5 (89.3, 99.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	6 (7.5)
Number of Subjects Censored, n (%)	41 (100.0)	74 (92.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.2, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.124

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	92.4 (86.5, 98.2)
6 months	100.0 (100.0, 100.0)	92.4 (86.5, 98.2)
9 months	NE (NE, NE)	92.4 (86.5, 98.2)
12 months	NE (NE, NE)	92.4 (86.5, 98.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	9 (22.0)	27 (33.8)
Number of Subjects Censored, n (%)	32 (78.0)	53 (66.3)
Time to first TEAE (months)		
25% percentile (95% CI)	2.83 (0.95, NE)	1.97 (0.95, 4.57)
Median (95% CI)	NE (NE, NE)	NE (4.57, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.1, 12.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.359 (0.392)
95% CI		(0.630, 2.931)
Log-rank p-value		0.496

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.4 (56.9, 89.9)	67.7 (56.9, 78.5)
6 months	73.4 (56.9, 89.9)	59.0 (45.7, 72.3)
9 months	NE (NE, NE)	59.0 (45.7, 72.3)
12 months	NE (NE, NE)	59.0 (45.7, 72.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	4 (9.8)	21 (26.3)
Number of Subjects Censored, n (%)	37 (90.2)	59 (73.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	2.99 (1.02, NE)
Median (95% CI)	NE (NE, NE)	NE (8.38, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.7, 12.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.631 (0.553)
95% CI		(0.891, 7.772)
Log-rank p-value		0.090

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.2 (81.0, 99.3)	72.3 (61.7, 82.8)
6 months	90.2 (81.0, 99.3)	72.3 (61.7, 82.8)
9 months	NE (NE, NE)	60.2 (36.9, 83.5)
12 months	NE (NE, NE)	60.2 (36.9, 83.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	4 (9.8)	20 (25.0)
Number of Subjects Censored, n (%)	37 (90.2)	60 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.27, NE)	5.52 (1.87, 6.93)
Median (95% CI)	NE (NE, NE)	NE (5.72, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 4.9*	0.1, 12.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.698 (0.571)
95% CI		(0.554, 5.205)
Log-rank p-value		0.319

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.6 (77.9, 99.4)	79.2 (69.6, 88.8)
6 months	NE (NE, NE)	61.9 (45.2, 78.7)
9 months	NE (NE, NE)	55.1 (35.5, 74.6)
12 months	NE (NE, NE)	55.1 (35.5, 74.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	1 (2.4)	7 (8.8)
Number of Subjects Censored, n (%)	40 (97.6)	73 (91.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.14, NE)	NE (5.75, NE)
Median (95% CI)	NE (4.14, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.2, 12.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.007 (1.122)
95% CI		(0.223, 18.080)
Log-rank p-value		0.355

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.8 (89.9, 99.8)
6 months	85.7 (59.8, 100.0)	86.4 (74.3, 98.4)
9 months	NE (NE, NE)	79.7 (63.0, 96.5)
12 months	NE (NE, NE)	79.7 (63.0, 96.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	1 (2.4)	4 (5.0)
Number of Subjects Censored, n (%)	40 (97.6)	76 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.7, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.128 (1.174)
95% CI		(0.113, 11.261)
Log-rank p-value		0.939

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.3 (89.2, 100.0)	97.1 (93.2, 100.0)
6 months	96.3 (89.2, 100.0)	91.1 (81.9, 100.0)
9 months	NE (NE, NE)	91.1 (81.9, 100.0)
12 months	NE (NE, NE)	91.1 (81.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	4 (5.0)
Number of Subjects Censored, n (%)	41 (100.0)	76 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.8*, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.242

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.3 (90.1, 100.0)
6 months	100.0 (100.0, 100.0)	91.4 (82.2, 100.0)
9 months	NE (NE, NE)	91.4 (82.2, 100.0)
12 months	NE (NE, NE)	91.4 (82.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	12 (29.3)	13 (16.3)
Number of Subjects Censored, n (%)	29 (70.7)	67 (83.8)
Time to first TEAE (months)		
25% percentile (95% CI)	1.61 (0.72, NE)	NE (3.75, NE)
Median (95% CI)	NE (2.79, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 5.6*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.391 (0.436)
95% CI		(0.166, 0.919)
Log-rank p-value		0.024

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	67.8 (52.0, 83.6)	86.4 (78.6, 94.3)
6 months	NE (NE, NE)	76.5 (63.5, 89.4)
9 months	NE (NE, NE)	76.5 (63.5, 89.4)
12 months	NE (NE, NE)	76.5 (63.5, 89.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	8 (19.5)	11 (13.8)
Number of Subjects Censored, n (%)	33 (80.5)	69 (86.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.02, NE)	NE (5.78, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.526 (0.514)
95% CI		(0.192, 1.440)
Log-rank p-value		0.171

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.9 (60.4, 91.4)	89.0 (81.7, 96.2)
6 months	NE (NE, NE)	78.8 (65.8, 91.7)
9 months	NE (NE, NE)	78.8 (65.8, 91.7)
12 months	NE (NE, NE)	78.8 (65.8, 91.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.20	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	1 (2.4)	2 (2.5)
Number of Subjects Censored, n (%)	40 (97.6)	78 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.8*, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.114 (1.230)
95% CI		(0.100, 12.402)
Log-rank p-value		0.889

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (91.6, 100.0)	97.4 (93.9, 100.0)
6 months	97.1 (91.6, 100.0)	97.4 (93.9, 100.0)
9 months	NE (NE, NE)	97.4 (93.9, 100.0)
12 months	NE (NE, NE)	97.4 (93.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Endocrine disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	23 (28.8)
Number of Subjects Censored, n (%)	41 (100.0)	57 (71.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	2.79 (1.41, 9.33)
Median (95% CI)	NE (NE, NE)	9.33 (5.78, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (9.33, NE)
Min, Max	1.0*, 8.4*	0.7, 12.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Endocrine disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	73.9 (63.7, 84.1)
6 months	100.0 (100.0, 100.0)	61.8 (46.2, 77.4)
9 months	NE (NE, NE)	61.8 (46.2, 77.4)
12 months	NE (NE, NE)	41.2 (6.6, 75.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	21 (26.3)
Number of Subjects Censored, n (%)	41 (100.0)	59 (73.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.84 (1.41, 9.33)
Median (95% CI)	NE (NE, NE)	9.33 (5.78, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (9.33, NE)
Min, Max	1.0*, 8.4*	0.7, 12.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	77.1 (67.5, 86.7)
6 months	100.0 (100.0, 100.0)	65.2 (50.0, 80.4)
9 months	NE (NE, NE)	65.2 (50.0, 80.4)
12 months	NE (NE, NE)	43.5 (7.2, 79.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	3 (7.3)	17 (21.3)
Number of Subjects Censored, n (%)	38 (92.7)	63 (78.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.72 (2.43, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 8.4*	0.1, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.818 (0.640)
95% CI		(0.804, 9.876)
Log-rank p-value		0.061

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.6 (82.3, 100.0)	77.2 (67.2, 87.2)
6 months	91.6 (82.3, 100.0)	72.6 (59.9, 85.4)
9 months	NE (NE, NE)	72.6 (59.9, 85.4)
12 months	NE (NE, NE)	72.6 (59.9, 85.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	2 (4.9)	8 (10.0)
Number of Subjects Censored, n (%)	39 (95.1)	72 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 8.4*	0.1, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.753 (0.794)
95% CI		(0.370, 8.312)
Log-rank p-value		0.365

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (88.5, 100.0)	87.4 (79.1, 95.7)
6 months	95.1 (88.5, 100.0)	87.4 (79.1, 95.7)
9 months	NE (NE, NE)	87.4 (79.1, 95.7)
12 months	NE (NE, NE)	87.4 (79.1, 95.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.19

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	1 (2.4)	4 (5.0)
Number of Subjects Censored, n (%)	40 (97.6)	76 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.7, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.022 (1.130)
95% CI		(0.221, 18.509)
Log-rank p-value		0.442

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (91.6, 100.0)	94.1 (88.3, 99.8)
6 months	97.1 (91.6, 100.0)	94.1 (88.3, 99.8)
9 months	NE (NE, NE)	94.1 (88.3, 99.8)
12 months	NE (NE, NE)	94.1 (88.3, 99.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	1 (2.4)	4 (5.0)
Number of Subjects Censored, n (%)	40 (97.6)	76 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.3, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.555 (1.182)
95% CI		(0.252, 25.919)
Log-rank p-value		0.489

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.6 (89.9, 100.0)	94.6 (89.4, 99.8)
6 months	96.6 (89.9, 100.0)	94.6 (89.4, 99.8)
9 months	NE (NE, NE)	94.6 (89.4, 99.8)
12 months	NE (NE, NE)	94.6 (89.4, 99.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	2 (4.9)	5 (6.3)
Number of Subjects Censored, n (%)	39 (95.1)	75 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.62, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 8.4*	0.1, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.791 (0.897)
95% CI		(0.136, 4.587)
Log-rank p-value		0.772

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (88.4, 100.0)	96.1 (91.7, 100.0)
6 months	95.1 (88.4, 100.0)	91.9 (82.9, 100.0)
9 months	NE (NE, NE)	84.2 (67.6, 100.0)
12 months	NE (NE, NE)	84.2 (67.6, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	0	1 (1.3)
Number of Subjects Censored, n (%)	41 (100.0)	79 (98.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 8.4*	0.8*, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.537

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.6 (95.8, 100.0)
6 months	100.0 (100.0, 100.0)	98.6 (95.8, 100.0)
9 months	NE (NE, NE)	98.6 (95.8, 100.0)
12 months	NE (NE, NE)	98.6 (95.8, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Number of Subjects with Events, n (%)	1 (2.4)	2 (2.5)
Number of Subjects Censored, n (%)	40 (97.6)	78 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.62, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 8.4*	0.1, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.596 (1.426)
95% CI		(0.036, 9.743)
Log-rank p-value		0.816

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
North America

Statistics	Placebo + BSC N=41	Fruquintinib + BSC N=80
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (92.8, 100.0)	98.8 (96.3, 100.0)
6 months	97.6 (92.8, 100.0)	98.8 (96.3, 100.0)
9 months	NE (NE, NE)	90.5 (74.9, 100.0)
12 months	NE (NE, NE)	90.5 (74.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	102 (61.1)	240 (73.4)
Number of Subjects Censored, n (%)	65 (38.9)	87 (26.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.46, 0.69)	0.36 (0.26, 0.66)
Median (95% CI)	1.58 (0.99, 2.50)	0.99 (0.72, 1.48)
75% percentile (95% CI)	NE (4.70, NE)	4.60 (3.71, 6.93)
Min, Max	0.0, 13.0*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.187 (0.120)
95% CI		(0.939, 1.501)
Log-rank p-value		0.210

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	38.7 (31.1, 46.4)	35.1 (29.8, 40.3)
6 months	30.6 (19.1, 42.2)	21.0 (15.6, 26.3)
9 months	30.6 (19.1, 42.2)	15.2 (8.9, 21.6)
12 months	30.6 (19.1, 42.2)	15.2 (8.9, 21.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.38	0.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	51 (30.5)	155 (47.4)
Number of Subjects Censored, n (%)	116 (69.5)	172 (52.6)
Time to first TEAE (months)		
25% percentile (95% CI)	1.28 (0.72, 3.22)	0.69 (0.69, 0.92)
Median (95% CI)	NE (4.70, NE)	4.76 (2.89, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.536 (0.163)
95% CI		(1.117, 2.112)
Log-rank p-value		0.009

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	68.9 (61.6, 76.3)	55.1 (49.6, 60.7)
6 months	60.8 (47.2, 74.3)	49.8 (43.9, 55.8)
9 months	60.8 (47.2, 74.3)	46.5 (39.1, 53.8)
12 months	60.8 (47.2, 74.3)	46.5 (39.1, 53.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.33	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	23 (13.8)	41 (12.5)
Number of Subjects Censored, n (%)	144 (86.2)	286 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.789 (0.263)
95% CI		(0.471, 1.323)
Log-rank p-value		0.377

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.9 (79.1, 90.6)	88.7 (85.2, 92.2)
6 months	84.9 (79.1, 90.6)	86.3 (82.2, 90.4)
9 months	84.9 (79.1, 90.6)	84.8 (79.9, 89.8)
12 months	84.9 (79.1, 90.6)	84.8 (79.9, 89.8)
18 months	NE (NE, NE)	84.8 (79.9, 89.8)
Median Follow-up Time (months)	2.79	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	16 (9.6)	34 (10.4)
Number of Subjects Censored, n (%)	151 (90.4)	293 (89.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.70, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.853 (0.310)
95% CI		(0.465, 1.566)
Log-rank p-value		0.578

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.7 (84.7, 94.8)	91.5 (88.4, 94.6)
6 months	83.3 (70.3, 96.3)	88.4 (84.3, 92.4)
9 months	83.3 (70.3, 96.3)	87.4 (82.9, 91.8)
12 months	83.3 (70.3, 96.3)	82.2 (71.6, 92.8)
18 months	NE (NE, NE)	82.2 (71.6, 92.8)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	6 (3.6)	56 (17.1)
Number of Subjects Censored, n (%)	161 (96.4)	271 (82.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.24 (7.26, NE)
Median (95% CI)	NE (NE, NE)	NE (13.24, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.24, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.572 (0.431)
95% CI		(1.963, 10.649)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.1 (93.0, 99.2)	84.8 (80.9, 88.7)
6 months	96.1 (93.0, 99.2)	82.5 (78.1, 86.9)
9 months	96.1 (93.0, 99.2)	79.5 (73.5, 85.4)
12 months	96.1 (93.0, 99.2)	79.5 (73.5, 85.4)
18 months	NE (NE, NE)	53.0 (10.4, 95.5)
Median Follow-up Time (months)	2.83	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	22 (13.2)	20 (6.1)
Number of Subjects Censored, n (%)	145 (86.8)	307 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.329 (0.318)
95% CI		(0.176, 0.613)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.6 (81.1, 92.2)	95.4 (93.1, 97.8)
6 months	82.1 (74.0, 90.3)	92.4 (89.0, 95.9)
9 months	82.1 (74.0, 90.3)	92.4 (89.0, 95.9)
12 months	82.1 (74.0, 90.3)	92.4 (89.0, 95.9)
18 months	NE (NE, NE)	85.3 (71.6, 99.1)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	10 (6.0)	14 (4.3)
Number of Subjects Censored, n (%)	157 (94.0)	313 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.597 (0.426)
95% CI		(0.259, 1.378)
Log-rank p-value		0.214

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.8 (90.2, 97.5)	96.2 (94.0, 98.3)
6 months	93.8 (90.2, 97.5)	96.2 (94.0, 98.3)
9 months	93.8 (90.2, 97.5)	93.5 (87.9, 99.1)
12 months	93.8 (90.2, 97.5)	89.9 (81.2, 98.6)
18 months	NE (NE, NE)	89.9 (81.2, 98.6)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	5 (3.0)	16 (4.9)
Number of Subjects Censored, n (%)	162 (97.0)	311 (95.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.82, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.922 (0.539)
95% CI		(0.321, 2.649)
Log-rank p-value		0.857

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.8 (94.0, 99.6)	97.5 (95.7, 99.2)
6 months	96.8 (94.0, 99.6)	95.1 (92.2, 98.0)
9 months	96.8 (94.0, 99.6)	93.5 (89.2, 97.7)
12 months	96.8 (94.0, 99.6)	84.5 (74.0, 94.9)
18 months	NE (NE, NE)	84.5 (74.0, 94.9)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	4 (2.4)	11 (3.4)
Number of Subjects Censored, n (%)	163 (97.6)	316 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.958 (0.600)
95% CI		(0.296, 3.101)
Log-rank p-value		0.939

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (93.9, 100.0)	97.3 (95.4, 99.2)
6 months	96.9 (93.9, 100.0)	96.0 (93.5, 98.6)
9 months	96.9 (93.9, 100.0)	94.4 (90.4, 98.4)
12 months	96.9 (93.9, 100.0)	94.4 (90.4, 98.4)
18 months	NE (NE, NE)	94.4 (90.4, 98.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	1 (0.6)	5 (1.5)
Number of Subjects Censored, n (%)	166 (99.4)	322 (98.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.367 (1.109)
95% CI		(0.269, 20.801)
Log-rank p-value		0.423

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	98.8 (97.6, 100.0)
6 months	99.4 (98.2, 100.0)	98.8 (97.6, 100.0)
9 months	99.4 (98.2, 100.0)	96.4 (91.6, 100.0)
12 months	99.4 (98.2, 100.0)	96.4 (91.6, 100.0)
18 months	NE (NE, NE)	96.4 (91.6, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	96 (57.5)	218 (66.7)
Number of Subjects Censored, n (%)	71 (42.5)	109 (33.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.53 (0.30, 0.69)	0.56 (0.46, 0.69)
Median (95% CI)	1.68 (1.15, 2.79)	1.51 (0.95, 2.04)
75% percentile (95% CI)	5.59 (5.36, NE)	7.62 (5.03, NE)
Min, Max	0.0, 6.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.034 (0.124)
95% CI		(0.810, 1.320)
Log-rank p-value		0.716

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	40.0 (31.8, 48.2)	40.0 (34.6, 45.5)
6 months	22.7 (5.6, 39.8)	27.9 (21.9, 34.0)
9 months	NE (NE, NE)	21.1 (14.1, 28.1)
12 months	NE (NE, NE)	18.1 (10.0, 26.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.31	1.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	15 (9.0)	80 (24.5)
Number of Subjects Censored, n (%)	152 (91.0)	247 (75.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.96 (2.53, 10.87)
Median (95% CI)	NE (NE, NE)	NE (10.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.491 (0.283)
95% CI		(1.429, 4.340)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.8 (86.3, 95.2)	78.9 (74.4, 83.4)
6 months	90.8 (86.3, 95.2)	71.6 (65.5, 77.7)
9 months	90.8 (86.3, 95.2)	69.3 (62.6, 76.0)
12 months	90.8 (86.3, 95.2)	63.0 (49.8, 76.3)
18 months	NE (NE, NE)	63.0 (49.8, 76.3)
Median Follow-up Time (months)	2.79	2.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	26 (15.6)	44 (13.5)
Number of Subjects Censored, n (%)	141 (84.4)	283 (86.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.31, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.614 (0.256)
95% CI		(0.372, 1.014)
Log-rank p-value		0.058

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.5 (77.6, 89.3)	89.1 (85.5, 92.6)
6 months	83.5 (77.6, 89.3)	85.1 (80.4, 89.7)
9 months	83.5 (77.6, 89.3)	81.3 (75.1, 87.5)
12 months	83.5 (77.6, 89.3)	76.0 (66.9, 85.2)
18 months	NE (NE, NE)	76.0 (66.9, 85.2)
Median Follow-up Time (months)	2.79	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	25 (15.0)	59 (18.0)
Number of Subjects Censored, n (%)	142 (85.0)	268 (82.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	9.23 (6.18, NE)
Median (95% CI)	NE (NE, NE)	NE (12.25, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.919 (0.245)
95% CI		(0.569, 1.485)
Log-rank p-value		0.781

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.8 (76.2, 89.3)	85.5 (81.5, 89.4)
6 months	82.8 (76.2, 89.3)	81.4 (76.5, 86.2)
9 months	82.8 (76.2, 89.3)	75.9 (68.9, 82.9)
12 months	82.8 (76.2, 89.3)	69.2 (58.1, 80.2)
18 months	NE (NE, NE)	60.5 (41.9, 79.1)
Median Follow-up Time (months)	2.79	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	13 (7.8)	51 (15.6)
Number of Subjects Censored, n (%)	154 (92.2)	276 (84.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.80, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.587 (0.315)
95% CI		(0.857, 2.941)
Log-rank p-value		0.149

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (85.5, 96.4)	86.7 (82.9, 90.5)
6 months	89.0 (82.4, 95.6)	81.8 (76.8, 86.7)
9 months	89.0 (82.4, 95.6)	80.4 (74.9, 86.0)
12 months	89.0 (82.4, 95.6)	77.4 (69.6, 85.3)
18 months	NE (NE, NE)	77.4 (69.6, 85.3)
Median Follow-up Time (months)	2.83	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	19 (11.4)	41 (12.5)
Number of Subjects Censored, n (%)	148 (88.6)	286 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.36, NE)	18.04 (7.39, NE)
Median (95% CI)	NE (NE, NE)	NE (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.737 (0.290)
95% CI		(0.418, 1.299)
Log-rank p-value		0.314

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.8 (83.7, 93.9)	90.6 (87.3, 93.9)
6 months	80.0 (66.6, 93.3)	87.2 (82.8, 91.5)
9 months	80.0 (66.6, 93.3)	82.2 (75.9, 88.5)
12 months	80.0 (66.6, 93.3)	76.3 (66.3, 86.2)
18 months	NE (NE, NE)	76.3 (66.3, 86.2)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	5 (3.0)	42 (12.8)
Number of Subjects Censored, n (%)	162 (97.0)	285 (87.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.066 (0.475)
95% CI		(1.602, 10.321)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.7 (93.9, 99.6)	88.2 (84.7, 91.7)
6 months	96.7 (93.9, 99.6)	87.0 (83.2, 90.9)
9 months	96.7 (93.9, 99.6)	84.2 (78.8, 89.6)
12 months	96.7 (93.9, 99.6)	84.2 (78.8, 89.6)
18 months	NE (NE, NE)	84.2 (78.8, 89.6)
Median Follow-up Time (months)	2.83	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	6 (3.6)	31 (9.5)
Number of Subjects Censored, n (%)	161 (96.4)	296 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.089 (0.452)
95% CI		(0.861, 5.069)
Log-rank p-value		0.100

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (94.2, 99.6)	92.4 (89.4, 95.3)
6 months	89.4 (75.2, 100.0)	88.5 (84.3, 92.7)
9 months	NE (NE, NE)	86.8 (81.5, 92.0)
12 months	NE (NE, NE)	86.8 (81.5, 92.0)
18 months	NE (NE, NE)	86.8 (81.5, 92.0)
Median Follow-up Time (months)	2.83	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	4 (2.4)	14 (4.3)
Number of Subjects Censored, n (%)	163 (97.6)	313 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.429 (0.578)
95% CI		(0.460, 4.440)
Log-rank p-value		0.517

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (94.9, 99.9)	96.6 (94.6, 98.6)
6 months	97.4 (94.9, 99.9)	95.0 (92.1, 98.0)
9 months	97.4 (94.9, 99.9)	93.4 (89.2, 97.7)
12 months	97.4 (94.9, 99.9)	93.4 (89.2, 97.7)
18 months	NE (NE, NE)	93.4 (89.2, 97.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	3 (1.8)	7 (2.1)
Number of Subjects Censored, n (%)	164 (98.2)	320 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.101 (0.691)
95% CI		(0.284, 4.263)
Log-rank p-value		0.905

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (95.9, 100.0)	97.8 (96.3, 99.4)
6 months	98.1 (95.9, 100.0)	97.8 (96.3, 99.4)
9 months	98.1 (95.9, 100.0)	97.8 (96.3, 99.4)
12 months	98.1 (95.9, 100.0)	97.8 (96.3, 99.4)
18 months	NE (NE, NE)	97.8 (96.3, 99.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	10 (6.0)	1 (0.3)
Number of Subjects Censored, n (%)	157 (94.0)	326 (99.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.047 (1.049)
95% CI		(0.006, 0.368)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.4 (89.5, 97.4)	99.7 (99.0, 100.0)
6 months	93.4 (89.5, 97.4)	99.7 (99.0, 100.0)
9 months	93.4 (89.5, 97.4)	99.7 (99.0, 100.0)
12 months	93.4 (89.5, 97.4)	99.7 (99.0, 100.0)
18 months	NE (NE, NE)	99.7 (99.0, 100.0)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	0	10 (3.1)
Number of Subjects Censored, n (%)	167 (100.0)	317 (96.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.035

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.1 (95.2, 99.0)
6 months	100.0 (100.0, 100.0)	97.1 (95.2, 99.0)
9 months	100.0 (100.0, 100.0)	95.4 (91.5, 99.2)
12 months	100.0 (100.0, 100.0)	95.4 (91.5, 99.2)
18 months	NE (NE, NE)	95.4 (91.5, 99.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	42 (25.1)	129 (39.4)
Number of Subjects Censored, n (%)	125 (74.9)	198 (60.6)
Time to first TEAE (months)		
25% percentile (95% CI)	1.91 (0.95, NE)	1.64 (1.08, 1.94)
Median (95% CI)	10.18 (NE, NE)	9.43 (6.05, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.0, 10.2	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.373 (0.179)
95% CI		(0.966, 1.952)
Log-rank p-value		0.060

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	74.9 (68.2, 81.7)	63.8 (58.3, 69.2)
6 months	72.9 (65.1, 80.6)	57.3 (51.1, 63.4)
9 months	72.9 (65.1, 80.6)	51.3 (43.8, 58.9)
12 months	0.0 (NE, NE)	47.4 (37.2, 57.6)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	30 (18.0)	90 (27.5)
Number of Subjects Censored, n (%)	137 (82.0)	237 (72.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.91, NE)	2.89 (1.84, 6.24)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.360 (0.213)
95% CI		(0.896, 2.065)
Log-rank p-value		0.147

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.7 (74.4, 86.9)	74.0 (69.0, 78.9)
6 months	80.7 (74.4, 86.9)	69.9 (64.4, 75.5)
9 months	80.7 (74.4, 86.9)	68.0 (62.0, 74.0)
12 months	80.7 (74.4, 86.9)	65.0 (57.0, 73.1)
18 months	NE (NE, NE)	65.0 (57.0, 73.1)
Median Follow-up Time (months)	2.69	2.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	3 (1.8)	11 (3.4)
Number of Subjects Censored, n (%)	164 (98.2)	316 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.554 (0.660)
95% CI		(0.427, 5.662)
Log-rank p-value		0.519

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (96.2, 100.0)	96.7 (94.7, 98.7)
6 months	98.2 (96.2, 100.0)	96.7 (94.7, 98.7)
9 months	98.2 (96.2, 100.0)	95.0 (91.2, 98.8)
12 months	98.2 (96.2, 100.0)	95.0 (91.2, 98.8)
18 months	NE (NE, NE)	95.0 (91.2, 98.8)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	1 (0.6)	6 (1.8)
Number of Subjects Censored, n (%)	166 (99.4)	321 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.020 (1.099)
95% CI		(0.234, 17.422)
Log-rank p-value		0.487

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.4 (97.0, 99.8)
6 months	97.8 (93.6, 100.0)	98.4 (97.0, 99.8)
9 months	97.8 (93.6, 100.0)	96.8 (93.5, 100.0)
12 months	97.8 (93.6, 100.0)	96.8 (93.5, 100.0)
18 months	NE (NE, NE)	96.8 (93.5, 100.0)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	1 (0.6)	7 (2.1)
Number of Subjects Censored, n (%)	166 (99.4)	320 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.665 (1.082)
95% CI		(0.320, 22.227)
Log-rank p-value		0.305

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	98.3 (96.9, 99.8)
6 months	99.4 (98.2, 100.0)	97.8 (95.9, 99.6)
9 months	99.4 (98.2, 100.0)	95.4 (90.4, 100.0)
12 months	99.4 (98.2, 100.0)	95.4 (90.4, 100.0)
18 months	NE (NE, NE)	95.4 (90.4, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	3 (1.8)	2 (0.6)
Number of Subjects Censored, n (%)	164 (98.2)	325 (99.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.310 (0.915)
95% CI		(0.052, 1.863)
Log-rank p-value		0.187

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (96.1, 100.0)	99.3 (98.4, 100.0)
6 months	98.2 (96.1, 100.0)	99.3 (98.4, 100.0)
9 months	98.2 (96.1, 100.0)	99.3 (98.4, 100.0)
12 months	98.2 (96.1, 100.0)	99.3 (98.4, 100.0)
18 months	NE (NE, NE)	99.3 (98.4, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	0	6 (1.8)
Number of Subjects Censored, n (%)	167 (100.0)	321 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.168

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.1 (98.0, 100.0)
6 months	100.0 (100.0, 100.0)	97.8 (95.9, 99.8)
9 months	100.0 (100.0, 100.0)	96.4 (93.0, 99.8)
12 months	100.0 (100.0, 100.0)	96.4 (93.0, 99.8)
18 months	NE (NE, NE)	96.4 (93.0, 99.8)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	0	2 (0.6)
Number of Subjects Censored, n (%)	167 (100.0)	325 (99.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.367

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.3 (98.3, 100.0)
6 months	100.0 (100.0, 100.0)	99.3 (98.3, 100.0)
9 months	100.0 (100.0, 100.0)	99.3 (98.3, 100.0)
12 months	100.0 (100.0, 100.0)	99.3 (98.3, 100.0)
18 months	NE (NE, NE)	99.3 (98.3, 100.0)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	1 (0.6)	9 (2.8)
Number of Subjects Censored, n (%)	166 (99.4)	318 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.827 (1.073)
95% CI		(0.345, 23.152)
Log-rank p-value		0.293

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	98.4 (97.0, 99.8)
6 months	99.4 (98.2, 100.0)	97.0 (94.6, 99.4)
9 months	99.4 (98.2, 100.0)	93.7 (88.3, 99.1)
12 months	99.4 (98.2, 100.0)	93.7 (88.3, 99.1)
18 months	NE (NE, NE)	93.7 (88.3, 99.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	3 (1.8)	3 (0.9)
Number of Subjects Censored, n (%)	164 (98.2)	324 (99.1)
Time to first TEAE (months)		
25% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Median (95% CI)	10.18 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 10.2	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.323 (0.901)
95% CI		(0.055, 1.890)
Log-rank p-value		0.229

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (97.1, 100.0)	99.1 (98.0, 100.0)
6 months	98.8 (97.1, 100.0)	99.1 (98.0, 100.0)
9 months	98.8 (97.1, 100.0)	99.1 (98.0, 100.0)
12 months	0.0 (NE, NE)	99.1 (98.0, 100.0)
18 months	0.0 (NE, NE)	99.1 (98.0, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	1 (0.6)	4 (1.2)
Number of Subjects Censored, n (%)	166 (99.4)	323 (98.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.018 (1.169)
95% CI		(0.103, 10.063)
Log-rank p-value		0.961

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	99.7 (99.1, 100.0)
6 months	99.3 (97.9, 100.0)	97.2 (94.4, 100.0)
9 months	99.3 (97.9, 100.0)	97.2 (94.4, 100.0)
12 months	99.3 (97.9, 100.0)	97.2 (94.4, 100.0)
18 months	NE (NE, NE)	97.2 (94.4, 100.0)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	39 (23.4)	113 (34.6)
Number of Subjects Censored, n (%)	128 (76.6)	214 (65.4)
Time to first TEAE (months)		
25% percentile (95% CI)	3.55 (1.58, NE)	2.23 (1.61, 2.83)
Median (95% CI)	NE (5.82, NE)	16.79 (6.67, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (16.79, NE)
Min, Max	0.2*, 6.8*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.237 (0.189)
95% CI		(0.854, 1.791)
Log-rank p-value		0.292

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.1 (70.5, 83.8)	69.4 (64.3, 74.6)
6 months	56.7 (33.3, 80.1)	62.5 (56.2, 68.7)
9 months	NE (NE, NE)	54.8 (47.1, 62.5)
12 months	NE (NE, NE)	54.8 (47.1, 62.5)
18 months	NE (NE, NE)	41.1 (17.1, 65.1)
Median Follow-up Time (months)	2.79	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	13 (7.8)	31 (9.5)
Number of Subjects Censored, n (%)	154 (92.2)	296 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	5.82 (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.82, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.888 (0.339)
95% CI		(0.457, 1.726)
Log-rank p-value		0.711

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.6 (86.8, 96.4)	91.7 (88.6, 94.9)
6 months	70.5 (42.7, 98.2)	88.2 (83.8, 92.5)
9 months	NE (NE, NE)	87.2 (82.5, 91.9)
12 months	NE (NE, NE)	87.2 (82.5, 91.9)
18 months	NE (NE, NE)	87.2 (82.5, 91.9)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	5 (3.0)	29 (8.9)
Number of Subjects Censored, n (%)	162 (97.0)	298 (91.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.173 (0.491)
95% CI		(0.829, 5.694)
Log-rank p-value		0.107

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (95.2, 99.9)	92.7 (89.8, 95.7)
6 months	90.0 (75.7, 100.0)	89.5 (85.5, 93.6)
9 months	NE (NE, NE)	87.4 (82.4, 92.3)
12 months	NE (NE, NE)	87.4 (82.4, 92.3)
18 months	NE (NE, NE)	87.4 (82.4, 92.3)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	4 (2.4)	29 (8.9)
Number of Subjects Censored, n (%)	163 (97.6)	298 (91.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.826 (0.540)
95% CI		(0.982, 8.138)
Log-rank p-value		0.046

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (96.1, 100.0)	92.8 (89.9, 95.7)
6 months	90.6 (76.3, 100.0)	89.6 (85.6, 93.6)
9 months	NE (NE, NE)	87.4 (82.4, 92.3)
12 months	NE (NE, NE)	87.4 (82.4, 92.3)
18 months	NE (NE, NE)	87.4 (82.4, 92.3)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	9 (5.4)	23 (7.0)
Number of Subjects Censored, n (%)	158 (94.6)	304 (93.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.968 (0.402)
95% CI		(0.440, 2.129)
Log-rank p-value		0.918

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.5 (90.9, 98.0)	94.8 (92.4, 97.3)
6 months	94.5 (90.9, 98.0)	91.9 (88.4, 95.4)
9 months	94.5 (90.9, 98.0)	89.2 (84.3, 94.2)
12 months	94.5 (90.9, 98.0)	89.2 (84.3, 94.2)
18 months	NE (NE, NE)	89.2 (84.3, 94.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	1 (0.6)	20 (6.1)
Number of Subjects Censored, n (%)	166 (99.4)	307 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		7.830 (1.031)
95% CI		(1.039, 59.027)
Log-rank p-value		0.020

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	94.7 (92.2, 97.2)
6 months	99.4 (98.2, 100.0)	93.7 (90.6, 96.9)
9 months	99.4 (98.2, 100.0)	89.4 (83.5, 95.4)
12 months	99.4 (98.2, 100.0)	89.4 (83.5, 95.4)
18 months	NE (NE, NE)	89.4 (83.5, 95.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	5 (3.0)	11 (3.4)
Number of Subjects Censored, n (%)	162 (97.0)	316 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.912 (0.550)
95% CI		(0.310, 2.681)
Log-rank p-value		0.916

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.8 (94.0, 99.6)	97.0 (95.1, 99.0)
6 months	96.8 (94.0, 99.6)	96.4 (94.2, 98.7)
9 months	96.8 (94.0, 99.6)	95.4 (92.4, 98.4)
12 months	96.8 (94.0, 99.6)	95.4 (92.4, 98.4)
18 months	NE (NE, NE)	95.4 (92.4, 98.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	1 (0.6)	11 (3.4)
Number of Subjects Censored, n (%)	166 (99.4)	316 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	7.43 (NE, NE)	NE (NE, NE)
Median (95% CI)	7.43 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	7.43 (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 7.4	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.811 (1.054)
95% CI		(0.483, 30.086)
Log-rank p-value		0.180

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.9 (94.8, 98.9)
6 months	100.0 (100.0, 100.0)	95.5 (92.7, 98.3)
9 months	0.0 (NE, NE)	95.5 (92.7, 98.3)
12 months	0.0 (NE, NE)	95.5 (92.7, 98.3)
18 months	0.0 (NE, NE)	95.5 (92.7, 98.3)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	1 (0.6)	10 (3.1)
Number of Subjects Censored, n (%)	166 (99.4)	317 (96.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.289 (1.053)
95% CI		(0.545, 33.768)
Log-rank p-value		0.134

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.1 (95.2, 99.0)
6 months	97.1 (91.4, 100.0)	96.5 (94.4, 98.7)
9 months	97.1 (91.4, 100.0)	96.5 (94.4, 98.7)
12 months	97.1 (91.4, 100.0)	96.5 (94.4, 98.7)
18 months	NE (NE, NE)	96.5 (94.4, 98.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	1 (0.6)	5 (1.5)
Number of Subjects Censored, n (%)	166 (99.4)	322 (98.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.757 (1.119)
95% CI		(0.196, 15.741)
Log-rank p-value		0.604

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	98.7 (97.4, 100.0)
6 months	99.4 (98.2, 100.0)	98.7 (97.4, 100.0)
9 months	99.4 (98.2, 100.0)	97.3 (94.4, 100.0)
12 months	99.4 (98.2, 100.0)	97.3 (94.4, 100.0)
18 months	NE (NE, NE)	97.3 (94.4, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	1 (0.6)	7 (2.1)
Number of Subjects Censored, n (%)	166 (99.4)	320 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.544 (1.081)
95% CI		(0.306, 21.153)
Log-rank p-value		0.371

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	98.0 (96.4, 99.6)
6 months	99.4 (98.2, 100.0)	98.0 (96.4, 99.6)
9 months	99.4 (98.2, 100.0)	96.6 (93.5, 99.7)
12 months	99.4 (98.2, 100.0)	96.6 (93.5, 99.7)
18 months	NE (NE, NE)	96.6 (93.5, 99.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	40 (24.0)	120 (36.7)
Number of Subjects Censored, n (%)	127 (76.0)	207 (63.3)
Time to first TEAE (months)		
25% percentile (95% CI)	2.53 (1.48, NE)	0.95 (0.69, 1.64)
Median (95% CI)	NE (NE, NE)	11.53 (9.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.456 (0.185)
95% CI		(1.014, 2.091)
Log-rank p-value		0.054

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	74.3 (67.3, 81.3)	66.7 (61.5, 71.8)
6 months	74.3 (67.3, 81.3)	61.2 (55.1, 67.2)
9 months	74.3 (67.3, 81.3)	59.2 (52.7, 65.6)
12 months	74.3 (67.3, 81.3)	48.2 (35.1, 61.3)
18 months	NE (NE, NE)	48.2 (35.1, 61.3)
Median Follow-up Time (months)	2.46	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	8 (4.8)	54 (16.5)
Number of Subjects Censored, n (%)	159 (95.2)	273 (83.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.661 (0.381)
95% CI		(1.734, 7.727)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.8 (91.3, 98.4)	83.2 (79.1, 87.3)
6 months	94.8 (91.3, 98.4)	83.2 (79.1, 87.3)
9 months	94.8 (91.3, 98.4)	83.2 (79.1, 87.3)
12 months	94.8 (91.3, 98.4)	83.2 (79.1, 87.3)
18 months	NE (NE, NE)	83.2 (79.1, 87.3)
Median Follow-up Time (months)	2.83	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	16 (9.6)	26 (8.0)
Number of Subjects Censored, n (%)	151 (90.4)	301 (92.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	14.32 (14.32, NE)
Median (95% CI)	NE (NE, NE)	NE (14.32, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.641 (0.327)
95% CI		(0.338, 1.216)
Log-rank p-value		0.161

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.9 (85.1, 94.6)	93.6 (90.8, 96.3)
6 months	89.9 (85.1, 94.6)	91.6 (88.1, 95.1)
9 months	89.9 (85.1, 94.6)	89.6 (85.2, 94.0)
12 months	89.9 (85.1, 94.6)	89.6 (85.2, 94.0)
18 months	NE (NE, NE)	74.7 (47.7, 100.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	16 (9.6)	26 (8.0)
Number of Subjects Censored, n (%)	151 (90.4)	301 (92.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.709 (0.324)
95% CI		(0.376, 1.337)
Log-rank p-value		0.275

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.6 (84.7, 94.5)	92.9 (90.0, 95.7)
6 months	89.6 (84.7, 94.5)	92.2 (89.1, 95.3)
9 months	89.6 (84.7, 94.5)	91.1 (87.5, 94.8)
12 months	89.6 (84.7, 94.5)	85.4 (74.1, 96.8)
18 months	NE (NE, NE)	85.4 (74.1, 96.8)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	2 (1.2)	8 (2.4)
Number of Subjects Censored, n (%)	165 (98.8)	319 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.678 (0.794)
95% CI		(0.354, 7.963)
Log-rank p-value		0.537

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (97.1, 100.0)	97.4 (95.6, 99.2)
6 months	98.8 (97.1, 100.0)	97.4 (95.6, 99.2)
9 months	98.8 (97.1, 100.0)	97.4 (95.6, 99.2)
12 months	98.8 (97.1, 100.0)	97.4 (95.6, 99.2)
18 months	NE (NE, NE)	97.4 (95.6, 99.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	1 (0.6)	4 (1.2)
Number of Subjects Censored, n (%)	166 (99.4)	323 (98.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.664 (1.139)
95% CI		(0.178, 15.522)
Log-rank p-value		0.662

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	99.1 (98.0, 100.0)
6 months	99.3 (97.8, 100.0)	98.3 (96.5, 100.0)
9 months	99.3 (97.8, 100.0)	98.3 (96.5, 100.0)
12 months	99.3 (97.8, 100.0)	98.3 (96.5, 100.0)
18 months	NE (NE, NE)	98.3 (96.5, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Vascular disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	23 (13.8)	131 (40.1)
Number of Subjects Censored, n (%)	144 (86.2)	196 (59.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.61, NE)	0.95 (0.69, 1.58)
Median (95% CI)	NE (NE, NE)	NE (6.93, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.184 (0.227)
95% CI		(2.039, 4.970)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Vascular disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.4 (79.7, 91.1)	60.7 (55.2, 66.1)
6 months	82.2 (73.8, 90.5)	57.4 (51.5, 63.3)
9 months	NE (NE, NE)	54.1 (47.0, 61.2)
12 months	NE (NE, NE)	54.1 (47.0, 61.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	2.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	16 (9.6)	124 (37.9)
Number of Subjects Censored, n (%)	151 (90.4)	203 (62.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.99 (0.72, 1.64)
Median (95% CI)	NE (NE, NE)	NE (7.13, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.324 (0.267)
95% CI		(2.563, 7.296)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.3 (84.3, 94.3)	63.1 (57.7, 68.5)
6 months	89.3 (84.3, 94.3)	59.7 (53.9, 65.6)
9 months	NE (NE, NE)	54.9 (47.4, 62.5)
12 months	NE (NE, NE)	54.9 (47.4, 62.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	2.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	36 (21.6)	107 (32.7)
Number of Subjects Censored, n (%)	131 (78.4)	220 (67.3)
Time to first TEAE (months)		
25% percentile (95% CI)	3.71 (1.87, NE)	1.68 (1.02, 2.76)
Median (95% CI)	NE (5.59, NE)	NE (8.64, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.359 (0.195)
95% CI		(0.927, 1.993)
Log-rank p-value		0.118

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.5 (70.7, 84.4)	69.5 (64.3, 74.6)
6 months	65.1 (46.4, 83.8)	63.3 (57.0, 69.6)
9 months	NE (NE, NE)	57.9 (49.6, 66.2)
12 months	NE (NE, NE)	57.9 (49.6, 66.2)
18 months	NE (NE, NE)	57.9 (49.6, 66.2)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	15 (9.0)	32 (9.8)
Number of Subjects Censored, n (%)	152 (91.0)	295 (90.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.865 (0.319)
95% CI		(0.463, 1.617)
Log-rank p-value		0.739

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.5 (86.0, 95.1)	91.1 (87.9, 94.3)
6 months	90.5 (86.0, 95.1)	88.3 (84.2, 92.5)
9 months	90.5 (86.0, 95.1)	87.3 (82.8, 91.9)
12 months	90.5 (86.0, 95.1)	87.3 (82.8, 91.9)
18 months	NE (NE, NE)	87.3 (82.8, 91.9)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	9 (5.4)	31 (9.5)
Number of Subjects Censored, n (%)	158 (94.6)	296 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.379 (0.385)
95% CI		(0.648, 2.935)
Log-rank p-value		0.401

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.0 (91.6, 98.4)	91.7 (88.6, 94.8)
6 months	87.7 (73.6, 100.0)	89.2 (85.0, 93.4)
9 months	NE (NE, NE)	85.8 (79.7, 91.9)
12 months	NE (NE, NE)	85.8 (79.7, 91.9)
18 months	NE (NE, NE)	85.8 (79.7, 91.9)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	2 (1.2)	20 (6.1)
Number of Subjects Censored, n (%)	165 (98.8)	307 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.566 (0.744)
95% CI		(1.061, 19.640)
Log-rank p-value		0.028

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	94.2 (91.6, 96.8)
6 months	96.4 (90.5, 100.0)	92.5 (89.1, 96.0)
9 months	96.4 (90.5, 100.0)	92.5 (89.1, 96.0)
12 months	96.4 (90.5, 100.0)	92.5 (89.1, 96.0)
18 months	NE (NE, NE)	92.5 (89.1, 96.0)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	2 (1.2)	9 (2.8)
Number of Subjects Censored, n (%)	165 (98.8)	318 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.968 (0.788)
95% CI		(0.420, 9.227)
Log-rank p-value		0.402

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (97.0, 100.0)	97.4 (95.7, 99.2)
6 months	98.7 (97.0, 100.0)	96.4 (93.8, 99.0)
9 months	98.7 (97.0, 100.0)	96.4 (93.8, 99.0)
12 months	98.7 (97.0, 100.0)	96.4 (93.8, 99.0)
18 months	NE (NE, NE)	96.4 (93.8, 99.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	1 (0.6)	10 (3.1)
Number of Subjects Censored, n (%)	166 (99.4)	317 (96.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.793 (1.063)
95% CI		(0.472, 30.458)
Log-rank p-value		0.189

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	97.8 (96.2, 99.4)
6 months	99.4 (98.2, 100.0)	96.9 (94.5, 99.3)
9 months	99.4 (98.2, 100.0)	92.9 (86.8, 98.9)
12 months	99.4 (98.2, 100.0)	92.9 (86.8, 98.9)
18 months	NE (NE, NE)	92.9 (86.8, 98.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	0	4 (1.2)
Number of Subjects Censored, n (%)	167 (100.0)	323 (98.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.209

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.6 (97.2, 100.0)
6 months	100.0 (100.0, 100.0)	98.6 (97.2, 100.0)
9 months	100.0 (100.0, 100.0)	98.6 (97.2, 100.0)
12 months	100.0 (100.0, 100.0)	98.6 (97.2, 100.0)
18 months	NE (NE, NE)	98.6 (97.2, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	17 (10.2)	104 (31.8)
Number of Subjects Censored, n (%)	150 (89.8)	223 (68.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.61 (1.05, 3.58)
Median (95% CI)	NE (NE, NE)	13.14 (13.14, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.14, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.067 (0.263)
95% CI		(1.833, 5.134)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (85.4, 94.7)	70.5 (65.5, 75.5)
6 months	86.8 (79.2, 94.5)	65.6 (59.8, 71.5)
9 months	86.8 (79.2, 94.5)	62.7 (55.8, 69.6)
12 months	86.8 (79.2, 94.5)	62.7 (55.8, 69.6)
18 months	NE (NE, NE)	47.1 (19.9, 74.2)
Median Follow-up Time (months)	2.79	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	3 (1.8)	59 (18.0)
Number of Subjects Censored, n (%)	164 (98.2)	268 (82.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.60, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		9.449 (0.593)
95% CI		(2.955, 30.214)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (96.1, 100.0)	83.9 (79.9, 88.0)
6 months	98.2 (96.1, 100.0)	79.1 (74.0, 84.3)
9 months	98.2 (96.1, 100.0)	77.4 (71.3, 83.5)
12 months	98.2 (96.1, 100.0)	77.4 (71.3, 83.5)
18 months	NE (NE, NE)	77.4 (71.3, 83.5)
Median Follow-up Time (months)	2.83	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	4 (2.4)	8 (2.4)
Number of Subjects Censored, n (%)	163 (97.6)	319 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.966 (0.615)
95% CI		(0.289, 3.227)
Log-rank p-value		0.951

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (95.2, 99.9)	97.5 (95.9, 99.2)
6 months	97.6 (95.2, 99.9)	97.5 (95.9, 99.2)
9 months	97.6 (95.2, 99.9)	97.5 (95.9, 99.2)
12 months	97.6 (95.2, 99.9)	97.5 (95.9, 99.2)
18 months	NE (NE, NE)	97.5 (95.9, 99.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	2 (1.2)	8 (2.4)
Number of Subjects Censored, n (%)	165 (98.8)	319 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.927 (0.794)
95% CI		(0.407, 9.135)
Log-rank p-value		0.422

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	97.5 (95.8, 99.2)
6 months	96.2 (90.1, 100.0)	97.5 (95.8, 99.2)
9 months	96.2 (90.1, 100.0)	97.5 (95.8, 99.2)
12 months	96.2 (90.1, 100.0)	97.5 (95.8, 99.2)
18 months	NE (NE, NE)	97.5 (95.8, 99.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	25 (15.0)	76 (23.2)
Number of Subjects Censored, n (%)	142 (85.0)	251 (76.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.32 (2.99, NE)
Median (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.349 (0.233)
95% CI		(0.854, 2.132)
Log-rank p-value		0.219

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.0 (78.1, 89.8)	79.7 (75.2, 84.1)
6 months	84.0 (78.1, 89.8)	73.5 (67.8, 79.2)
9 months	84.0 (78.1, 89.8)	72.5 (66.5, 78.5)
12 months	84.0 (78.1, 89.8)	68.4 (58.9, 78.0)
18 months	NE (NE, NE)	68.4 (58.9, 78.0)
Median Follow-up Time (months)	2.79	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	7 (4.2)	27 (8.3)
Number of Subjects Censored, n (%)	160 (95.8)	300 (91.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
Median (95% CI)	NE (NE, NE)	NE (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.804 (0.428)
95% CI		(0.779, 4.174)
Log-rank p-value		0.175

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.2 (91.7, 98.7)	92.6 (89.7, 95.4)
6 months	95.2 (91.7, 98.7)	91.9 (88.7, 95.0)
9 months	95.2 (91.7, 98.7)	90.8 (87.1, 94.5)
12 months	95.2 (91.7, 98.7)	90.8 (87.1, 94.5)
18 months	NE (NE, NE)	90.8 (87.1, 94.5)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	7 (4.2)	4 (1.2)
Number of Subjects Censored, n (%)	160 (95.8)	323 (98.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.260 (0.631)
95% CI		(0.075, 0.895)
Log-rank p-value		0.021

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (92.6, 98.8)	98.7 (97.5, 100.0)
6 months	95.7 (92.6, 98.8)	98.7 (97.5, 100.0)
9 months	95.7 (92.6, 98.8)	98.7 (97.5, 100.0)
12 months	95.7 (92.6, 98.8)	98.7 (97.5, 100.0)
18 months	NE (NE, NE)	98.7 (97.5, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	4 (2.4)	5 (1.5)
Number of Subjects Censored, n (%)	163 (97.6)	322 (98.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.611 (0.672)
95% CI		(0.164, 2.280)
Log-rank p-value		0.489

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (94.9, 99.9)	98.4 (97.0, 99.8)
6 months	97.4 (94.9, 99.9)	98.4 (97.0, 99.8)
9 months	97.4 (94.9, 99.9)	98.4 (97.0, 99.8)
12 months	97.4 (94.9, 99.9)	98.4 (97.0, 99.8)
18 months	NE (NE, NE)	98.4 (97.0, 99.8)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	19 (11.4)	62 (19.0)
Number of Subjects Censored, n (%)	148 (88.6)	265 (81.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	11.96 (4.63, NE)
Median (95% CI)	NE (NE, NE)	NE (11.96, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.2*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.349 (0.266)
95% CI		(0.800, 2.273)
Log-rank p-value		0.269

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (82.2, 92.8)	84.0 (79.9, 88.1)
6 months	87.5 (82.2, 92.8)	80.0 (75.2, 84.9)
9 months	87.5 (82.2, 92.8)	76.2 (69.9, 82.5)
12 months	87.5 (82.2, 92.8)	67.7 (51.1, 84.3)
18 months	NE (NE, NE)	50.8 (19.5, 82.1)
Median Follow-up Time (months)	2.79	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	7 (4.2)	36 (11.0)
Number of Subjects Censored, n (%)	160 (95.8)	291 (89.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.60 (13.60, NE)
Median (95% CI)	NE (NE, NE)	NE (13.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.161 (0.417)
95% CI		(0.954, 4.896)
Log-rank p-value		0.049

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (92.0, 98.7)	91.0 (87.8, 94.2)
6 months	95.4 (92.0, 98.7)	87.6 (83.6, 91.7)
9 months	95.4 (92.0, 98.7)	86.2 (81.3, 91.1)
12 months	95.4 (92.0, 98.7)	86.2 (81.3, 91.1)
18 months	NE (NE, NE)	64.6 (27.9, 100.0)
Median Follow-up Time (months)	2.83	3.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	5 (3.0)	7 (2.1)
Number of Subjects Censored, n (%)	162 (97.0)	320 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.498 (0.607)
95% CI		(0.151, 1.637)
Log-rank p-value		0.248

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.8 (94.0, 99.6)	98.1 (96.6, 99.6)
6 months	96.8 (94.0, 99.6)	97.5 (95.6, 99.4)
9 months	96.8 (94.0, 99.6)	97.5 (95.6, 99.4)
12 months	96.8 (94.0, 99.6)	97.5 (95.6, 99.4)
18 months	NE (NE, NE)	97.5 (95.6, 99.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	22 (13.2)	63 (19.3)
Number of Subjects Censored, n (%)	145 (86.8)	264 (80.7)
Time to first TEAE (months)		
25% percentile (95% CI)	5.78 (3.71, NE)	6.54 (4.63, 17.48)
Median (95% CI)	NE (5.78, NE)	17.48 (17.48, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.48, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.023 (0.255)
95% CI		(0.621, 1.686)
Log-rank p-value		0.786

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.4 (83.3, 93.5)	86.0 (82.1, 89.9)
6 months	67.3 (44.4, 90.2)	78.2 (72.5, 83.8)
9 months	67.3 (44.4, 90.2)	70.2 (62.2, 78.2)
12 months	67.3 (44.4, 90.2)	65.2 (53.1, 77.2)
18 months	NE (NE, NE)	48.9 (19.8, 78.0)
Median Follow-up Time (months)	2.83	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	6 (3.6)	11 (3.4)
Number of Subjects Censored, n (%)	161 (96.4)	316 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.711 (0.522)
95% CI		(0.255, 1.977)
Log-rank p-value		0.571

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (95.2, 99.9)	97.1 (95.2, 99.0)
6 months	92.6 (85.3, 99.8)	97.1 (95.2, 99.0)
9 months	92.6 (85.3, 99.8)	95.0 (91.5, 98.4)
12 months	92.6 (85.3, 99.8)	95.0 (91.5, 98.4)
18 months	NE (NE, NE)	95.0 (91.5, 98.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	5 (3.0)	8 (2.4)
Number of Subjects Censored, n (%)	162 (97.0)	319 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (11.56, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.371 (0.622)
95% CI		(0.110, 1.256)
Log-rank p-value		0.119

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (95.0, 99.9)	98.9 (97.8, 100.0)
6 months	92.6 (83.0, 100.0)	97.1 (94.6, 99.5)
9 months	92.6 (83.0, 100.0)	95.9 (92.6, 99.2)
12 months	92.6 (83.0, 100.0)	90.3 (79.1, 100.0)
18 months	NE (NE, NE)	90.3 (79.1, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	1 (0.6)	6 (1.8)
Number of Subjects Censored, n (%)	166 (99.4)	321 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.824 (1.082)
95% CI		(0.339, 23.545)
Log-rank p-value		0.325

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	98.1 (96.5, 99.6)
6 months	99.4 (98.2, 100.0)	98.1 (96.5, 99.6)
9 months	99.4 (98.2, 100.0)	98.1 (96.5, 99.6)
12 months	99.4 (98.2, 100.0)	98.1 (96.5, 99.6)
18 months	NE (NE, NE)	98.1 (96.5, 99.6)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	25 (15.0)	50 (15.3)
Number of Subjects Censored, n (%)	142 (85.0)	277 (84.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.77, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.839 (0.249)
95% CI		(0.515, 1.366)
Log-rank p-value		0.485

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.2 (77.2, 89.3)	86.1 (82.2, 90.0)
6 months	83.2 (77.2, 89.3)	83.6 (79.1, 88.1)
9 months	83.2 (77.2, 89.3)	80.0 (74.1, 85.9)
12 months	83.2 (77.2, 89.3)	80.0 (74.1, 85.9)
18 months	NE (NE, NE)	80.0 (74.1, 85.9)
Median Follow-up Time (months)	2.79	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	20 (12.0)	24 (7.3)
Number of Subjects Censored, n (%)	147 (88.0)	303 (92.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	17.74 (17.74, NE)
Median (95% CI)	NE (NE, NE)	NE (17.74, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.74, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.412 (0.315)
95% CI		(0.223, 0.764)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.5 (80.9, 92.1)	94.7 (92.2, 97.2)
6 months	86.5 (80.9, 92.1)	91.4 (87.7, 95.2)
9 months	86.5 (80.9, 92.1)	89.4 (84.7, 94.0)
12 months	86.5 (80.9, 92.1)	89.4 (84.7, 94.0)
18 months	NE (NE, NE)	59.6 (11.8, 100.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	2 (1.2)	26 (8.0)
Number of Subjects Censored, n (%)	165 (98.8)	301 (92.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.528 (0.735)
95% CI		(1.547, 27.554)
Log-rank p-value		0.004

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (97.1, 100.0)	91.6 (88.6, 94.7)
6 months	98.8 (97.1, 100.0)	91.6 (88.6, 94.7)
9 months	98.8 (97.1, 100.0)	91.6 (88.6, 94.7)
12 months	98.8 (97.1, 100.0)	91.6 (88.6, 94.7)
18 months	NE (NE, NE)	91.6 (88.6, 94.7)
Median Follow-up Time (months)	2.83	3.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Endocrine disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	1 (0.6)	62 (19.0)
Number of Subjects Censored, n (%)	166 (99.4)	265 (81.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.98 (4.37, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		25.600 (1.009)
95% CI		(3.542, 185.026)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Endocrine disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	84.2 (80.1, 88.3)
6 months	99.4 (98.2, 100.0)	74.5 (68.0, 81.0)
9 months	99.4 (98.2, 100.0)	71.8 (64.5, 79.1)
12 months	99.4 (98.2, 100.0)	71.8 (64.5, 79.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	1 (0.6)	59 (18.0)
Number of Subjects Censored, n (%)	166 (99.4)	268 (82.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	6.90 (5.52, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		23.867 (1.010)
95% CI		(3.298, 172.724)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	85.1 (81.1, 89.2)
6 months	99.4 (98.2, 100.0)	76.2 (69.9, 82.5)
9 months	99.4 (98.2, 100.0)	71.8 (64.1, 79.5)
12 months	99.4 (98.2, 100.0)	71.8 (64.1, 79.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	12 (7.2)	36 (11.0)
Number of Subjects Censored, n (%)	155 (92.8)	291 (89.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.100 (0.339)
95% CI		(0.565, 2.139)
Log-rank p-value		0.810

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.8 (88.7, 96.9)	91.2 (87.9, 94.5)
6 months	90.9 (85.5, 96.4)	85.5 (80.8, 90.3)
9 months	90.9 (85.5, 96.4)	84.3 (79.1, 89.6)
12 months	90.9 (85.5, 96.4)	84.3 (79.1, 89.6)
18 months	NE (NE, NE)	84.3 (79.1, 89.6)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	8 (4.8)	15 (4.6)
Number of Subjects Censored, n (%)	159 (95.2)	312 (95.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.612 (0.453)
95% CI		(0.252, 1.487)
Log-rank p-value		0.254

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.7 (91.0, 98.3)	96.5 (94.3, 98.6)
6 months	94.7 (91.0, 98.3)	94.0 (90.8, 97.2)
9 months	94.7 (91.0, 98.3)	92.7 (88.7, 96.7)
12 months	94.7 (91.0, 98.3)	92.7 (88.7, 96.7)
18 months	NE (NE, NE)	92.7 (88.7, 96.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	1 (0.6)	7 (2.1)
Number of Subjects Censored, n (%)	166 (99.4)	320 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.678 (1.076)
95% CI		(0.325, 22.075)
Log-rank p-value		0.356

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.9 (96.3, 99.6)
6 months	98.0 (94.1, 100.0)	97.1 (94.9, 99.4)
9 months	98.0 (94.1, 100.0)	97.1 (94.9, 99.4)
12 months	98.0 (94.1, 100.0)	97.1 (94.9, 99.4)
18 months	NE (NE, NE)	97.1 (94.9, 99.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	1 (0.6)	5 (1.5)
Number of Subjects Censored, n (%)	166 (99.4)	322 (98.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.999 (1.107)
95% CI		(0.228, 17.494)
Log-rank p-value		0.524

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	98.7 (97.4, 100.0)
6 months	99.4 (98.2, 100.0)	97.8 (95.7, 99.9)
9 months	99.4 (98.2, 100.0)	97.8 (95.7, 99.9)
12 months	99.4 (98.2, 100.0)	97.8 (95.7, 99.9)
18 months	NE (NE, NE)	97.8 (95.7, 99.9)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	22 (13.2)	42 (12.8)
Number of Subjects Censored, n (%)	145 (86.8)	285 (87.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.66, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.746 (0.267)
95% CI		(0.442, 1.261)
Log-rank p-value		0.260

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.8 (81.5, 92.1)	88.4 (84.7, 92.0)
6 months	84.9 (78.7, 91.2)	84.5 (79.9, 89.2)
9 months	84.9 (78.7, 91.2)	84.5 (79.9, 89.2)
12 months	84.9 (78.7, 91.2)	81.7 (74.6, 88.8)
18 months	NE (NE, NE)	81.7 (74.6, 88.8)
Median Follow-up Time (months)	2.83	3.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	3 (1.8)	18 (5.5)
Number of Subjects Censored, n (%)	164 (98.2)	309 (94.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.254 (0.630)
95% CI		(0.656, 7.745)
Log-rank p-value		0.213

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.9 (95.6, 100.0)	94.8 (92.2, 97.4)
6 months	97.9 (95.6, 100.0)	93.3 (90.0, 96.6)
9 months	97.9 (95.6, 100.0)	93.3 (90.0, 96.6)
12 months	97.9 (95.6, 100.0)	90.2 (83.4, 97.0)
18 months	NE (NE, NE)	90.2 (83.4, 97.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Number of Subjects with Events, n (%)	1 (0.6)	12 (3.7)
Number of Subjects Censored, n (%)	166 (99.4)	315 (96.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.653 (1.046)
95% CI		(0.599, 36.156)
Log-rank p-value		0.111

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Europe

Statistics	Placebo + BSC N=167	Fruquintinib + BSC N=327
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	96.8 (94.8, 98.7)
6 months	99.4 (98.2, 100.0)	95.3 (92.4, 98.1)
9 months	99.4 (98.2, 100.0)	95.3 (92.4, 98.1)
12 months	99.4 (98.2, 100.0)	95.3 (92.4, 98.1)
18 months	NE (NE, NE)	95.3 (92.4, 98.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	5 (22.7)	21 (42.9)
Number of Subjects Censored, n (%)	17 (77.3)	28 (57.1)
Time to first TEAE (months)		
25% percentile (95% CI)	2.37 (0.23, NE)	0.49 (0.23, 2.30)
Median (95% CI)	NE (2.37, NE)	NE (2.30, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.5*	0.1, 11.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.124 (0.509)
95% CI		(0.782, 5.764)
Log-rank p-value		0.102

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	74.8 (55.1, 94.4)	58.8 (44.9, 72.7)
6 months	74.8 (55.1, 94.4)	53.9 (38.2, 69.6)
9 months	NE (NE, NE)	53.9 (38.2, 69.6)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	1 (4.5)	7 (14.3)
Number of Subjects Censored, n (%)	21 (95.5)	42 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.36, NE)	NE (2.30, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 6.5*	0.1, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.231 (1.093)
95% CI		(0.379, 27.541)
Log-rank p-value		0.267

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (86.8, 100.0)	87.6 (78.2, 96.9)
6 months	95.5 (86.8, 100.0)	82.4 (69.2, 95.6)
9 months	NE (NE, NE)	82.4 (69.2, 95.6)
12 months	NE (NE, NE)	82.4 (69.2, 95.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	1 (4.5)	4 (8.2)
Number of Subjects Censored, n (%)	21 (95.5)	45 (91.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.39, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 6.5*	0.1, 11.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.670 (1.141)
95% CI		(0.285, 24.970)
Log-rank p-value		0.427

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (86.8, 100.0)	91.8 (84.2, 99.5)
6 months	95.5 (86.8, 100.0)	91.8 (84.2, 99.5)
9 months	NE (NE, NE)	91.8 (84.2, 99.5)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	2 (4.1)
Number of Subjects Censored, n (%)	22 (100.0)	47 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.5, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.415

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.7 (89.8, 100.0)
6 months	100.0 (100.0, 100.0)	95.7 (89.8, 100.0)
9 months	NE (NE, NE)	95.7 (89.8, 100.0)
12 months	NE (NE, NE)	95.7 (89.8, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	2 (9.1)	4 (8.2)
Number of Subjects Censored, n (%)	20 (90.9)	45 (91.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.27, NE)	NE (5.95, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.293 (1.007)
95% CI		(0.041, 2.106)
Log-rank p-value		0.120

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.7 (67.4, 100.0)	95.9 (90.4, 100.0)
6 months	85.7 (67.4, 100.0)	87.0 (74.0, 100.0)
9 months	NE (NE, NE)	87.0 (74.0, 100.0)
12 months	NE (NE, NE)	87.0 (74.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	3 (6.1)
Number of Subjects Censored, n (%)	22 (100.0)	46 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.5, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.174

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.5 (86.4, 100.0)
6 months	100.0 (100.0, 100.0)	93.5 (86.4, 100.0)
9 months	NE (NE, NE)	93.5 (86.4, 100.0)
12 months	NE (NE, NE)	93.5 (86.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	10 (45.5)	27 (55.1)
Number of Subjects Censored, n (%)	12 (54.5)	22 (44.9)
Time to first TEAE (months)		
25% percentile (95% CI)	1.45 (0.16, 3.75)	0.69 (0.26, 1.87)
Median (95% CI)	3.75 (1.45, NE)	4.40 (1.87, 6.70)
75% percentile (95% CI)	4.34 (3.75, NE)	6.70 (4.90, NE)
Min, Max	0.2, 4.3	0.1, 9.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.879 (0.413)
95% CI		(0.391, 1.975)
Log-rank p-value		0.870

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	63.6 (43.5, 83.7)	54.5 (39.6, 69.4)
6 months	0.0 (NE, NE)	33.5 (16.0, 51.0)
9 months	0.0 (NE, NE)	22.3 (1.0, 43.7)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	1 (4.5)	9 (18.4)
Number of Subjects Censored, n (%)	21 (95.5)	40 (81.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.46, NE)	NE (0.85, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 6.5*	0.1, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.947 (1.057)
95% CI		(0.498, 31.305)
Log-rank p-value		0.165

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (86.8, 100.0)	81.6 (70.7, 92.5)
6 months	95.5 (86.8, 100.0)	81.6 (70.7, 92.5)
9 months	NE (NE, NE)	81.6 (70.7, 92.5)
12 months	NE (NE, NE)	81.6 (70.7, 92.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	3.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	2 (9.1)	7 (14.3)
Number of Subjects Censored, n (%)	20 (90.9)	42 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (0.39, NE)	NE (5.55, NE)
Median (95% CI)	4.34 (4.34, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (4.34, NE)	NE (NE, NE)
Min, Max	0.4, 6.5*	0.1, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.822 (0.866)
95% CI		(0.150, 4.489)
Log-rank p-value		0.810

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (86.8, 100.0)	89.7 (81.1, 98.2)
6 months	47.7 (0.0, 100.0)	79.1 (63.4, 94.8)
9 months	NE (NE, NE)	79.1 (63.4, 94.8)
12 months	NE (NE, NE)	79.1 (63.4, 94.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	1 (4.5)	1 (2.0)
Number of Subjects Censored, n (%)	21 (95.5)	48 (98.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.61, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.535 (1.484)
95% CI		(0.029, 9.805)
Log-rank p-value		0.659

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.2 (86.1, 100.0)	97.9 (93.9, 100.0)
6 months	95.2 (86.1, 100.0)	97.9 (93.9, 100.0)
9 months	NE (NE, NE)	97.9 (93.9, 100.0)
12 months	NE (NE, NE)	97.9 (93.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	8 (16.3)
Number of Subjects Censored, n (%)	22 (100.0)	41 (83.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	6.70 (3.19, NE)
Median (95% CI)	NE (NE, NE)	NE (6.70, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.341

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	92.7 (84.7, 100.0)
6 months	100.0 (100.0, 100.0)	81.3 (66.8, 95.7)
9 months	NE (NE, NE)	62.7 (37.2, 88.2)
12 months	NE (NE, NE)	62.7 (37.2, 88.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	1 (4.5)	3 (6.1)
Number of Subjects Censored, n (%)	21 (95.5)	46 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.16, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.5*	0.4, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.780 (1.197)
95% CI		(0.075, 8.158)
Log-rank p-value		0.980

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (86.8, 100.0)	93.8 (87.0, 100.0)
6 months	95.5 (86.8, 100.0)	93.8 (87.0, 100.0)
9 months	NE (NE, NE)	93.8 (87.0, 100.0)
12 months	NE (NE, NE)	93.8 (87.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	2 (9.1)	8 (16.3)
Number of Subjects Censored, n (%)	20 (90.9)	41 (83.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (1.61, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	0.3, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.760 (0.801)
95% CI		(0.366, 8.461)
Log-rank p-value		0.460

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.7 (78.4, 100.0)	85.5 (75.5, 95.4)
6 months	90.7 (78.4, 100.0)	79.4 (64.6, 94.1)
9 months	NE (NE, NE)	79.4 (64.6, 94.1)
12 months	NE (NE, NE)	79.4 (64.6, 94.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.32	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	1 (2.0)
Number of Subjects Censored, n (%)	22 (100.0)	48 (98.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.3, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.602

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.0 (94.0, 100.0)
6 months	100.0 (100.0, 100.0)	98.0 (94.0, 100.0)
9 months	NE (NE, NE)	98.0 (94.0, 100.0)
12 months	NE (NE, NE)	98.0 (94.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	1 (2.0)
Number of Subjects Censored, n (%)	22 (100.0)	48 (98.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.683

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.7 (93.3, 100.0)
6 months	100.0 (100.0, 100.0)	97.7 (93.3, 100.0)
9 months	NE (NE, NE)	97.7 (93.3, 100.0)
12 months	NE (NE, NE)	97.7 (93.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	5 (22.7)	18 (36.7)
Number of Subjects Censored, n (%)	17 (77.3)	31 (63.3)
Time to first TEAE (months)		
25% percentile (95% CI)	4.27 (0.23, NE)	1.54 (0.53, 5.55)
Median (95% CI)	4.27 (4.27, NE)	NE (5.16, NE)
75% percentile (95% CI)	NE (4.27, NE)	NE (NE, NE)
Min, Max	0.2, 6.5*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.160 (0.532)
95% CI		(0.409, 3.289)
Log-rank p-value		0.738

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.8 (65.7, 97.9)	69.0 (55.9, 82.0)
6 months	40.9 (0.0, 98.2)	59.8 (43.4, 76.2)
9 months	NE (NE, NE)	54.8 (37.1, 72.5)
12 months	NE (NE, NE)	54.8 (37.1, 72.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	4 (18.2)	8 (16.3)
Number of Subjects Censored, n (%)	18 (81.8)	41 (83.7)
Time to first TEAE (months)		
25% percentile (95% CI)	4.27 (0.23, NE)	NE (0.69, NE)
Median (95% CI)	4.27 (4.27, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (4.27, NE)	NE (NE, NE)
Min, Max	0.2, 6.5*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.778 (0.626)
95% CI		(0.228, 2.655)
Log-rank p-value		0.613

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.4 (72.0, 100.0)	82.4 (71.0, 93.7)
6 months	43.2 (0.0, 100.0)	82.4 (71.0, 93.7)
9 months	NE (NE, NE)	82.4 (71.0, 93.7)
12 months	NE (NE, NE)	82.4 (71.0, 93.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	5 (10.2)
Number of Subjects Censored, n (%)	22 (100.0)	44 (89.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.174

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	89.3 (80.4, 98.2)
6 months	100.0 (100.0, 100.0)	89.3 (80.4, 98.2)
9 months	NE (NE, NE)	89.3 (80.4, 98.2)
12 months	NE (NE, NE)	89.3 (80.4, 98.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	1 (2.0)
Number of Subjects Censored, n (%)	22 (100.0)	48 (98.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.763

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	100.0 (100.0, 100.0)	96.3 (89.2, 100.0)
9 months	NE (NE, NE)	96.3 (89.2, 100.0)
12 months	NE (NE, NE)	96.3 (89.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	1 (4.5)	2 (4.1)
Number of Subjects Censored, n (%)	21 (95.5)	47 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	0.7, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.002 (1.314)
95% CI		(0.076, 13.174)
Log-rank p-value		0.792

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (86.8, 100.0)	95.9 (90.3, 100.0)
6 months	95.5 (86.8, 100.0)	95.9 (90.3, 100.0)
9 months	NE (NE, NE)	95.9 (90.3, 100.0)
12 months	NE (NE, NE)	95.9 (90.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	4 (8.2)
Number of Subjects Censored, n (%)	22 (100.0)	45 (91.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.16, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.5, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.242

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.7 (86.8, 100.0)
6 months	100.0 (100.0, 100.0)	88.5 (76.6, 100.0)
9 months	NE (NE, NE)	88.5 (76.6, 100.0)
12 months	NE (NE, NE)	88.5 (76.6, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	1 (2.0)
Number of Subjects Censored, n (%)	22 (100.0)	48 (98.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.480

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.9 (93.7, 100.0)
6 months	100.0 (100.0, 100.0)	97.9 (93.7, 100.0)
9 months	NE (NE, NE)	97.9 (93.7, 100.0)
12 months	NE (NE, NE)	97.9 (93.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	1 (2.0)
Number of Subjects Censored, n (%)	22 (100.0)	48 (98.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.617

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.9 (93.9, 100.0)
6 months	100.0 (100.0, 100.0)	97.9 (93.9, 100.0)
9 months	NE (NE, NE)	97.9 (93.9, 100.0)
12 months	NE (NE, NE)	97.9 (93.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	1 (2.0)
Number of Subjects Censored, n (%)	22 (100.0)	48 (98.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.655

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.7 (93.3, 100.0)
6 months	100.0 (100.0, 100.0)	97.7 (93.3, 100.0)
9 months	NE (NE, NE)	97.7 (93.3, 100.0)
12 months	NE (NE, NE)	97.7 (93.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	7 (31.8)	20 (40.8)
Number of Subjects Censored, n (%)	15 (68.2)	29 (59.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.89 (0.69, NE)	0.72 (0.69, 2.53)
Median (95% CI)	NE (0.89, NE)	NE (2.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	0.3, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.111 (0.456)
95% CI		(0.455, 2.716)
Log-rank p-value		0.978

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	67.9 (48.2, 87.5)	62.6 (48.8, 76.3)
6 months	67.9 (48.2, 87.5)	59.4 (45.1, 73.8)
9 months	NE (NE, NE)	55.7 (40.5, 70.9)
12 months	NE (NE, NE)	55.7 (40.5, 70.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.12	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	2 (4.1)
Number of Subjects Censored, n (%)	22 (100.0)	47 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.7, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.405

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.7 (89.8, 100.0)
6 months	100.0 (100.0, 100.0)	95.7 (89.8, 100.0)
9 months	NE (NE, NE)	95.7 (89.8, 100.0)
12 months	NE (NE, NE)	95.7 (89.8, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	4 (18.2)	4 (8.2)
Number of Subjects Censored, n (%)	18 (81.8)	45 (91.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	0.3, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.399 (0.736)
95% CI		(0.094, 1.691)
Log-rank p-value		0.140

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.6 (65.2, 97.9)	91.8 (84.1, 99.5)
6 months	81.6 (65.2, 97.9)	91.8 (84.1, 99.5)
9 months	NE (NE, NE)	91.8 (84.1, 99.5)
12 months	NE (NE, NE)	91.8 (84.1, 99.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	3 (13.6)	5 (10.2)
Number of Subjects Censored, n (%)	19 (86.4)	44 (89.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	0.7, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.654 (0.757)
95% CI		(0.148, 2.884)
Log-rank p-value		0.440

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.4 (72.0, 100.0)	89.5 (80.7, 98.2)
6 months	86.4 (72.0, 100.0)	89.5 (80.7, 98.2)
9 months	NE (NE, NE)	89.5 (80.7, 98.2)
12 months	NE (NE, NE)	89.5 (80.7, 98.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	1 (4.5)	4 (8.2)
Number of Subjects Censored, n (%)	21 (95.5)	45 (91.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	0.4, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.956 (1.166)
95% CI		(0.097, 9.396)
Log-rank p-value		0.856

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (86.8, 100.0)	93.7 (86.8, 100.0)
6 months	95.5 (86.8, 100.0)	90.2 (80.8, 99.7)
9 months	NE (NE, NE)	90.2 (80.8, 99.7)
12 months	NE (NE, NE)	90.2 (80.8, 99.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	3 (6.1)
Number of Subjects Censored, n (%)	22 (100.0)	46 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.229

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.6 (86.5, 100.0)
6 months	100.0 (100.0, 100.0)	93.6 (86.5, 100.0)
9 months	NE (NE, NE)	93.6 (86.5, 100.0)
12 months	NE (NE, NE)	93.6 (86.5, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	1 (4.5)	0
Number of Subjects Censored, n (%)	21 (95.5)	49 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.145

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (86.8, 100.0)	100.0 (100.0, 100.0)
6 months	95.5 (86.8, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	7 (14.3)
Number of Subjects Censored, n (%)	22 (100.0)	42 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.5, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.062

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	85.7 (75.8, 95.5)
6 months	100.0 (100.0, 100.0)	85.7 (75.8, 95.5)
9 months	NE (NE, NE)	85.7 (75.8, 95.5)
12 months	NE (NE, NE)	85.7 (75.8, 95.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	2 (9.1)	2 (4.1)
Number of Subjects Censored, n (%)	20 (90.9)	47 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (6.01, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.141 (1.290)
95% CI		(0.011, 1.762)
Log-rank p-value		0.036

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (78.9, 100.0)	97.9 (93.9, 100.0)
6 months	90.9 (78.9, 100.0)	97.9 (93.9, 100.0)
9 months	NE (NE, NE)	92.2 (80.6, 100.0)
12 months	NE (NE, NE)	92.2 (80.6, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	2 (4.1)
Number of Subjects Censored, n (%)	22 (100.0)	47 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.519

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.3 (89.1, 100.0)
6 months	100.0 (100.0, 100.0)	95.3 (89.1, 100.0)
9 months	NE (NE, NE)	95.3 (89.1, 100.0)
12 months	NE (NE, NE)	95.3 (89.1, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	1 (4.5)	2 (4.1)
Number of Subjects Censored, n (%)	21 (95.5)	47 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.792 (1.241)
95% CI		(0.070, 9.026)
Log-rank p-value		0.800

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (86.8, 100.0)	95.6 (89.6, 100.0)
6 months	95.5 (86.8, 100.0)	95.6 (89.6, 100.0)
9 months	NE (NE, NE)	95.6 (89.6, 100.0)
12 months	NE (NE, NE)	95.6 (89.6, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	4 (18.2)	20 (40.8)
Number of Subjects Censored, n (%)	18 (81.8)	29 (59.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.33, NE)	1.38 (0.26, 1.87)
Median (95% CI)	NE (2.76, NE)	NE (1.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 5.5*	0.1, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.151 (0.629)
95% CI		(0.919, 10.807)
Log-rank p-value		0.053

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.5 (56.8, 98.2)	62.3 (48.5, 76.2)
6 months	NE (NE, NE)	59.2 (44.8, 73.6)
9 months	NE (NE, NE)	53.3 (36.3, 70.3)
12 months	NE (NE, NE)	53.3 (36.3, 70.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.32	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	2 (9.1)	10 (20.4)
Number of Subjects Censored, n (%)	20 (90.9)	39 (79.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (0.26, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	0.1, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.431 (0.780)
95% CI		(0.527, 11.219)
Log-rank p-value		0.263

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.7 (78.4, 100.0)	79.6 (68.3, 90.9)
6 months	90.7 (78.4, 100.0)	79.6 (68.3, 90.9)
9 months	NE (NE, NE)	79.6 (68.3, 90.9)
12 months	NE (NE, NE)	79.6 (68.3, 90.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	1 (4.5)	2 (4.1)
Number of Subjects Censored, n (%)	21 (95.5)	47 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.33, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 6.5*	0.2, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.876 (1.245)
95% CI		(0.076, 10.039)
Log-rank p-value		0.922

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (86.8, 100.0)	95.8 (90.1, 100.0)
6 months	95.5 (86.8, 100.0)	95.8 (90.1, 100.0)
9 months	NE (NE, NE)	95.8 (90.1, 100.0)
12 months	NE (NE, NE)	95.8 (90.1, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	1 (4.5)	4 (8.2)
Number of Subjects Censored, n (%)	21 (95.5)	45 (91.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 5.5*	0.5, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		>999 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.161

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (86.8, 100.0)	91.6 (83.6, 99.5)
6 months	NE (NE, NE)	91.6 (83.6, 99.5)
9 months	NE (NE, NE)	91.6 (83.6, 99.5)
12 months	NE (NE, NE)	91.6 (83.6, 99.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	1 (2.0)
Number of Subjects Censored, n (%)	22 (100.0)	48 (98.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.34, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	93.3 (80.7, 100.0)
12 months	NE (NE, NE)	93.3 (80.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Vascular disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	3 (13.6)	22 (44.9)
Number of Subjects Censored, n (%)	19 (86.4)	27 (55.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	0.69 (0.16, 1.18)
Median (95% CI)	NE (NE, NE)	7.39 (1.18, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (7.39, NE)
Min, Max	0.6, 6.5*	0.0, 9.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.042 (0.623)
95% CI		(1.192, 13.701)
Log-rank p-value		0.016

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Vascular disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.9 (71.0, 100.0)	56.6 (42.6, 70.6)
6 months	85.9 (71.0, 100.0)	56.6 (42.6, 70.6)
9 months	NE (NE, NE)	42.5 (16.2, 68.7)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.09	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	2 (9.1)	22 (44.9)
Number of Subjects Censored, n (%)	20 (90.9)	27 (55.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	0.69 (0.16, 1.18)
Median (95% CI)	NE (NE, NE)	7.39 (1.18, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (7.39, NE)
Min, Max	0.6, 6.5*	0.0, 9.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.991 (0.745)
95% CI		(1.392, 25.781)
Log-rank p-value		0.007

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (78.9, 100.0)	56.6 (42.6, 70.6)
6 months	90.9 (78.9, 100.0)	56.6 (42.6, 70.6)
9 months	NE (NE, NE)	42.5 (16.2, 68.7)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.32	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	3 (13.6)	11 (22.4)
Number of Subjects Censored, n (%)	19 (86.4)	38 (77.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.16, NE)	6.74 (1.61, NE)
Median (95% CI)	NE (NE, NE)	NE (6.74, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.5*	0.3, 9.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.253 (0.689)
95% CI		(0.324, 4.835)
Log-rank p-value		0.615

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.4 (72.0, 100.0)	78.8 (67.1, 90.5)
6 months	86.4 (72.0, 100.0)	78.8 (67.1, 90.5)
9 months	NE (NE, NE)	70.9 (52.9, 89.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	3.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	3 (6.1)
Number of Subjects Censored, n (%)	22 (100.0)	46 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.295

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.6 (86.5, 100.0)
6 months	100.0 (100.0, 100.0)	93.6 (86.5, 100.0)
9 months	NE (NE, NE)	93.6 (86.5, 100.0)
12 months	NE (NE, NE)	93.6 (86.5, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	5 (10.2)
Number of Subjects Censored, n (%)	22 (100.0)	44 (89.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.74, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.4, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.209

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	91.6 (83.8, 99.5)
6 months	100.0 (100.0, 100.0)	91.6 (83.8, 99.5)
9 months	NE (NE, NE)	83.3 (66.2, 100.0)
12 months	NE (NE, NE)	83.3 (66.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	1 (4.5)	0
Number of Subjects Censored, n (%)	21 (95.5)	49 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.91, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.157

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.1 (82.9, 100.0)	100.0 (100.0, 100.0)
6 months	94.1 (82.9, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	1 (4.5)	1 (2.0)
Number of Subjects Censored, n (%)	21 (95.5)	48 (98.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.16, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.170 (1.521)
95% CI		(0.009, 3.347)
Log-rank p-value		0.307

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (86.8, 100.0)	97.9 (93.7, 100.0)
6 months	95.5 (86.8, 100.0)	97.9 (93.7, 100.0)
9 months	NE (NE, NE)	97.9 (93.7, 100.0)
12 months	NE (NE, NE)	97.9 (93.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	1 (4.5)	0
Number of Subjects Censored, n (%)	21 (95.5)	49 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.056

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (86.8, 100.0)	100.0 (100.0, 100.0)
6 months	95.5 (86.8, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	1 (2.0)
Number of Subjects Censored, n (%)	22 (100.0)	48 (98.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.508

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.8 (93.6, 100.0)
6 months	100.0 (100.0, 100.0)	97.8 (93.6, 100.0)
9 months	NE (NE, NE)	97.8 (93.6, 100.0)
12 months	NE (NE, NE)	97.8 (93.6, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	4 (18.2)	28 (57.1)
Number of Subjects Censored, n (%)	18 (81.8)	21 (42.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.23, NE)	0.49 (0.26, 1.38)
Median (95% CI)	NE (NE, NE)	2.04 (0.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (4.99, NE)
Min, Max	0.2, 6.5*	0.1, 9.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.597 (0.542)
95% CI		(1.243, 10.415)
Log-rank p-value		0.016

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.6 (65.2, 97.9)	42.6 (28.0, 57.2)
6 months	81.6 (65.2, 97.9)	34.1 (15.1, 53.0)
9 months	NE (NE, NE)	34.1 (15.1, 53.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	1.87

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	3 (13.6)	18 (36.7)
Number of Subjects Censored, n (%)	19 (86.4)	31 (63.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.23, NE)	0.69 (0.26, 2.30)
Median (95% CI)	NE (NE, NE)	NE (1.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.5*	0.1, 9.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.097 (0.629)
95% CI		(0.902, 10.631)
Log-rank p-value		0.059

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.1 (71.5, 100.0)	62.8 (49.2, 76.5)
6 months	86.1 (71.5, 100.0)	62.8 (49.2, 76.5)
9 months	NE (NE, NE)	62.8 (49.2, 76.5)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.14	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	2 (9.1)	6 (12.2)
Number of Subjects Censored, n (%)	20 (90.9)	43 (87.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.89, NE)	NE (2.99, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9, 6.5*	0.3, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.202 (0.847)
95% CI		(0.228, 6.324)
Log-rank p-value		0.943

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (78.9, 100.0)	86.6 (76.4, 96.8)
6 months	90.9 (78.9, 100.0)	86.6 (76.4, 96.8)
9 months	NE (NE, NE)	86.6 (76.4, 96.8)
12 months	NE (NE, NE)	86.6 (76.4, 96.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	1 (2.0)
Number of Subjects Censored, n (%)	22 (100.0)	48 (98.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.617

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.7 (93.3, 100.0)
6 months	100.0 (100.0, 100.0)	97.7 (93.3, 100.0)
9 months	NE (NE, NE)	97.7 (93.3, 100.0)
12 months	NE (NE, NE)	97.7 (93.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	3 (13.6)	10 (20.4)
Number of Subjects Censored, n (%)	19 (86.4)	39 (79.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.20, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.5*	0.2, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.172 (0.681)
95% CI		(0.309, 4.453)
Log-rank p-value		0.976

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.4 (72.0, 100.0)	81.5 (70.6, 92.4)
6 months	86.4 (72.0, 100.0)	77.5 (64.5, 90.4)
9 months	NE (NE, NE)	77.5 (64.5, 90.4)
12 months	NE (NE, NE)	77.5 (64.5, 90.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.32	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	3 (6.1)
Number of Subjects Censored, n (%)	22 (100.0)	46 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.63, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.2, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.297

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.9 (90.4, 100.0)
6 months	100.0 (100.0, 100.0)	91.4 (81.1, 100.0)
9 months	NE (NE, NE)	91.4 (81.1, 100.0)
12 months	NE (NE, NE)	91.4 (81.1, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	2 (4.1)
Number of Subjects Censored, n (%)	22 (100.0)	47 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.7, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.493

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.9 (90.3, 100.0)
6 months	100.0 (100.0, 100.0)	95.9 (90.3, 100.0)
9 months	NE (NE, NE)	95.9 (90.3, 100.0)
12 months	NE (NE, NE)	95.9 (90.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	1 (2.0)
Number of Subjects Censored, n (%)	22 (100.0)	48 (98.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.9 (93.9, 100.0)
6 months	100.0 (100.0, 100.0)	97.9 (93.9, 100.0)
9 months	NE (NE, NE)	97.9 (93.9, 100.0)
12 months	NE (NE, NE)	97.9 (93.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	2 (9.1)	23 (46.9)
Number of Subjects Censored, n (%)	20 (90.9)	26 (53.1)
Time to first TEAE (months)		
25% percentile (95% CI)	3.71 (0.69, NE)	1.61 (0.69, 2.83)
Median (95% CI)	NE (3.71, NE)	5.06 (2.79, NE)
75% percentile (95% CI)	NE (3.71, NE)	NE (5.55, NE)
Min, Max	0.7, 6.5*	0.2, 9.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.133 (0.754)
95% CI		(0.942, 18.129)
Log-rank p-value		0.083

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (86.8, 100.0)	61.7 (47.7, 75.7)
6 months	71.6 (30.6, 100.0)	33.7 (13.1, 54.4)
9 months	NE (NE, NE)	33.7 (13.1, 54.4)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	1 (4.5)	22 (44.9)
Number of Subjects Censored, n (%)	21 (95.5)	27 (55.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	1.61 (0.69, 2.83)
Median (95% CI)	NE (NE, NE)	5.06 (2.79, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (5.78, NE)
Min, Max	0.7, 6.5*	0.2, 9.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		9.162 (1.032)
95% CI		(1.213, 69.230)
Log-rank p-value		0.024

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (86.8, 100.0)	61.7 (47.7, 75.7)
6 months	95.5 (86.8, 100.0)	40.5 (20.4, 60.6)
9 months	NE (NE, NE)	40.5 (20.4, 60.6)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	3 (6.1)
Number of Subjects Censored, n (%)	22 (100.0)	46 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.4, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.390

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.8 (87.0, 100.0)
6 months	100.0 (100.0, 100.0)	93.8 (87.0, 100.0)
9 months	NE (NE, NE)	93.8 (87.0, 100.0)
12 months	NE (NE, NE)	93.8 (87.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	3 (13.6)	13 (26.5)
Number of Subjects Censored, n (%)	19 (86.4)	36 (73.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.13, NE)	5.78 (0.76, 8.21)
Median (95% CI)	NE (NE, NE)	8.21 (7.92, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (8.21, NE)
Min, Max	0.1, 6.5*	0.3, 11.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.929 (0.697)
95% CI		(0.237, 3.642)
Log-rank p-value		0.958

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.4 (72.0, 100.0)	82.8 (71.8, 93.8)
6 months	86.4 (72.0, 100.0)	72.0 (57.0, 87.1)
9 months	NE (NE, NE)	49.4 (21.1, 77.7)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	3.81

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	1 (4.5)	1 (2.0)
Number of Subjects Censored, n (%)	21 (95.5)	48 (98.0)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (4.34, NE)	NE (NE, NE)
Median (95% CI)	NE (4.34, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (4.34, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.000 (>999)
95% CI		(0.000, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	50.0 (0.0, 100.0)	96.4 (89.6, 100.0)
9 months	NE (NE, NE)	96.4 (89.6, 100.0)
12 months	NE (NE, NE)	96.4 (89.6, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	1 (2.0)
Number of Subjects Censored, n (%)	22 (100.0)	48 (98.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.705

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.1 (91.4, 100.0)
6 months	100.0 (100.0, 100.0)	97.1 (91.4, 100.0)
9 months	NE (NE, NE)	97.1 (91.4, 100.0)
12 months	NE (NE, NE)	97.1 (91.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	4 (8.2)
Number of Subjects Censored, n (%)	22 (100.0)	45 (91.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.63, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.7, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.195

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.8 (87.0, 100.0)
6 months	100.0 (100.0, 100.0)	89.5 (79.1, 100.0)
9 months	NE (NE, NE)	89.5 (79.1, 100.0)
12 months	NE (NE, NE)	89.5 (79.1, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	1 (2.0)
Number of Subjects Censored, n (%)	22 (100.0)	48 (98.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.9 (93.9, 100.0)
6 months	100.0 (100.0, 100.0)	97.9 (93.9, 100.0)
9 months	NE (NE, NE)	97.9 (93.9, 100.0)
12 months	NE (NE, NE)	97.9 (93.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	2 (4.1)
Number of Subjects Censored, n (%)	22 (100.0)	47 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.7, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.390

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.9 (90.3, 100.0)
6 months	100.0 (100.0, 100.0)	95.9 (90.3, 100.0)
9 months	NE (NE, NE)	95.9 (90.3, 100.0)
12 months	NE (NE, NE)	95.9 (90.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Endocrine disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	15 (30.6)
Number of Subjects Censored, n (%)	22 (100.0)	34 (69.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.65 (1.84, 6.47)
Median (95% CI)	NE (NE, NE)	NE (4.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 9.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.034

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Endocrine disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	80.6 (69.2, 92.0)
6 months	100.0 (100.0, 100.0)	62.2 (45.3, 79.0)
9 months	NE (NE, NE)	55.3 (35.6, 75.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	14 (28.6)
Number of Subjects Censored, n (%)	22 (100.0)	35 (71.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.71 (1.87, 6.47)
Median (95% CI)	NE (NE, NE)	NE (4.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 9.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.041

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	82.7 (71.8, 93.6)
6 months	100.0 (100.0, 100.0)	63.8 (46.8, 80.8)
9 months	NE (NE, NE)	56.7 (36.7, 76.7)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	2 (9.1)	5 (10.2)
Number of Subjects Censored, n (%)	20 (90.9)	44 (89.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.46, NE)	NE (3.75, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 6.5*	0.1, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.795 (0.882)
95% CI		(0.141, 4.477)
Log-rank p-value		0.815

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (78.9, 100.0)	91.7 (84.0, 99.5)
6 months	90.9 (78.9, 100.0)	88.6 (78.9, 98.2)
9 months	NE (NE, NE)	88.6 (78.9, 98.2)
12 months	NE (NE, NE)	88.6 (78.9, 98.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	2 (9.1)	3 (6.1)
Number of Subjects Censored, n (%)	20 (90.9)	46 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.46, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.368 (1.001)
95% CI		(0.052, 2.617)
Log-rank p-value		0.263

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (78.9, 100.0)	95.8 (90.2, 100.0)
6 months	90.9 (78.9, 100.0)	92.6 (84.4, 100.0)
9 months	NE (NE, NE)	92.6 (84.4, 100.0)
12 months	NE (NE, NE)	92.6 (84.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	4.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	2 (4.1)
Number of Subjects Censored, n (%)	22 (100.0)	47 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.602

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.9 (93.9, 100.0)
6 months	100.0 (100.0, 100.0)	94.7 (87.2, 100.0)
9 months	NE (NE, NE)	94.7 (87.2, 100.0)
12 months	NE (NE, NE)	94.7 (87.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3D
Summary of Time to Onset of TEAE by SOC/PT by Geographic Region
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Asia

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Number of Subjects with Events, n (%)	0	3 (6.1)
Number of Subjects Censored, n (%)	22 (100.0)	46 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.5*	0.9*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.287

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
ECOG: 0

Statistics	Placebo + BSC N=22	Fruquintinib + BSC N=49
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.5 (86.4, 100.0)
6 months	100.0 (100.0, 100.0)	93.5 (86.4, 100.0)
9 months	NE (NE, NE)	93.5 (86.4, 100.0)
12 months	NE (NE, NE)	93.5 (86.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	53 (52.0)	121 (62.7)
Number of Subjects Censored, n (%)	49 (48.0)	72 (37.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.36, 0.95)	0.36 (0.23, 0.69)
Median (95% CI)	2.76 (1.61, NE)	1.61 (0.95, 3.65)
75% percentile (95% CI)	NE (4.70, NE)	NE (6.47, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Min, Max	0.0, 6.4*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.259 (0.167)
95% CI		(0.906, 1.748)
Log-rank p-value		0.201

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	49.4 (39.4, 59.4)	44.7 (37.7, 51.8)
6 months	36.0 (19.7, 52.3)	33.7 (26.2, 41.3)
9 months	NE (NE, NE)	30.0 (21.6, 38.4)
12 months	NE (NE, NE)	30.0 (21.6, 38.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	1.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	17 (16.7)	56 (29.0)
Number of Subjects Censored, n (%)	85 (83.3)	137 (71.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.70, NE)	2.60 (1.18, 8.41)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.721 (0.280)
95% CI		(0.995, 2.977)
Log-rank p-value		0.055

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.1 (76.9, 91.2)	73.6 (67.3, 79.9)
6 months	76.4 (60.7, 92.1)	70.7 (64.0, 77.4)
9 months	NE (NE, NE)	65.5 (55.8, 75.2)
12 months	NE (NE, NE)	65.5 (55.8, 75.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	21 (20.6)	40 (20.7)
Number of Subjects Censored, n (%)	81 (79.4)	153 (79.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.48, NE)	NE (3.68, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.897 (0.275)
95% CI		(0.524, 1.537)
Log-rank p-value		0.680

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.7 (70.6, 86.8)	82.2 (76.8, 87.7)
6 months	78.7 (70.6, 86.8)	78.5 (72.4, 84.6)
9 months	NE (NE, NE)	76.6 (69.6, 83.6)
12 months	NE (NE, NE)	76.6 (69.6, 83.6)
18 months	NE (NE, NE)	76.6 (69.6, 83.6)
Median Follow-up Time (months)	2.83	4.47

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	10 (9.8)	19 (9.8)
Number of Subjects Censored, n (%)	92 (90.2)	174 (90.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.70, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.785 (0.407)
95% CI		(0.354, 1.744)
Log-rank p-value		0.480

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.3 (84.3, 96.4)	92.7 (89.0, 96.4)
6 months	82.1 (65.8, 98.4)	90.0 (85.3, 94.7)
9 months	NE (NE, NE)	88.6 (83.3, 94.0)
12 months	NE (NE, NE)	80.6 (64.7, 96.4)
18 months	NE (NE, NE)	80.6 (64.7, 96.4)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	3 (2.9)	26 (13.5)
Number of Subjects Censored, n (%)	99 (97.1)	167 (86.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
Median (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.24, NE)
Min, Max	0.4*, 8.4*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.707 (0.614)
95% CI		(1.412, 15.687)
Log-rank p-value		0.006

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.0 (93.6, 100.0)	88.0 (83.5, 92.6)
6 months	97.0 (93.6, 100.0)	88.0 (83.5, 92.6)
9 months	NE (NE, NE)	84.2 (77.3, 91.0)
12 months	NE (NE, NE)	84.2 (77.3, 91.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.63

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	7 (6.9)	7 (3.6)
Number of Subjects Censored, n (%)	95 (93.1)	186 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.8*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.300 (0.561)
95% CI		(0.100, 0.902)
Log-rank p-value		0.030

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.3 (88.1, 98.5)	98.9 (97.5, 100.0)
6 months	90.4 (82.9, 98.0)	94.6 (90.4, 98.7)
9 months	NE (NE, NE)	94.6 (90.4, 98.7)
12 months	NE (NE, NE)	94.6 (90.4, 98.7)
18 months	NE (NE, NE)	94.6 (90.4, 98.7)
Median Follow-up Time (months)	2.83	4.93

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	4 (3.9)	6 (3.1)
Number of Subjects Censored, n (%)	98 (96.1)	187 (96.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.99, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.653 (0.673)
95% CI		(0.175, 2.441)
Log-rank p-value		0.534

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.0 (92.2, 99.8)	97.4 (95.2, 99.7)
6 months	96.0 (92.2, 99.8)	97.4 (95.2, 99.7)
9 months	NE (NE, NE)	97.4 (95.2, 99.7)
12 months	NE (NE, NE)	92.3 (82.3, 100.0)
18 months	NE (NE, NE)	92.3 (82.3, 100.0)
Median Follow-up Time (months)	2.83	4.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	1 (1.0)	5 (2.6)
Number of Subjects Censored, n (%)	101 (99.0)	188 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.00, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.8*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.563 (1.264)
95% CI		(0.047, 6.698)
Log-rank p-value		0.678

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.0, 100.0)	100.0 (100.0, 100.0)
6 months	99.0 (97.0, 100.0)	98.3 (96.0, 100.0)
9 months	NE (NE, NE)	96.0 (91.0, 100.0)
12 months	NE (NE, NE)	86.8 (73.9, 99.8)
18 months	NE (NE, NE)	86.8 (73.9, 99.8)
Median Follow-up Time (months)	2.83	4.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	1 (1.0)	3 (1.6)
Number of Subjects Censored, n (%)	101 (99.0)	190 (98.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.8*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.622 (1.224)
95% CI		(0.057, 6.846)
Log-rank p-value		0.669

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.1, 100.0)	99.4 (98.3, 100.0)
6 months	99.0 (97.1, 100.0)	98.6 (96.5, 100.0)
9 months	NE (NE, NE)	96.3 (91.6, 100.0)
12 months	NE (NE, NE)	96.3 (91.6, 100.0)
18 months	NE (NE, NE)	96.3 (91.6, 100.0)
Median Follow-up Time (months)	2.83	4.93

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	1 (1.0)	6 (3.1)
Number of Subjects Censored, n (%)	101 (99.0)	187 (96.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.176 (1.096)
95% CI		(0.371, 27.192)
Log-rank p-value		0.267

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.1, 100.0)	97.4 (95.1, 99.6)
6 months	99.0 (97.1, 100.0)	97.4 (95.1, 99.6)
9 months	NE (NE, NE)	93.8 (86.5, 100.0)
12 months	NE (NE, NE)	93.8 (86.5, 100.0)
18 months	NE (NE, NE)	93.8 (86.5, 100.0)
Median Follow-up Time (months)	2.83	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	54 (52.9)	132 (68.4)
Number of Subjects Censored, n (%)	48 (47.1)	61 (31.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.36, 0.92)	0.69 (0.46, 0.69)
Median (95% CI)	2.00 (1.45, NE)	1.87 (1.25, 2.76)
75% percentile (95% CI)	NE (4.34, NE)	6.70 (4.70, NE)
Min, Max	0.0, 6.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.196 (0.166)
95% CI		(0.865, 1.655)
Log-rank p-value		0.247

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	46.9 (36.8, 56.9)	41.2 (34.1, 48.2)
6 months	38.2 (24.5, 51.9)	25.7 (18.2, 33.3)
9 months	NE (NE, NE)	19.9 (11.7, 28.2)
12 months	NE (NE, NE)	19.9 (11.7, 28.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.82	1.64

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	14 (13.7)	51 (26.4)
Number of Subjects Censored, n (%)	88 (86.3)	142 (73.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.88 (1.84, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.794 (0.306)
95% CI		(0.985, 3.267)
Log-rank p-value		0.064

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.0 (79.2, 92.8)	76.8 (70.7, 82.8)
6 months	86.0 (79.2, 92.8)	70.6 (63.1, 78.0)
9 months	NE (NE, NE)	69.1 (61.2, 76.9)
12 months	NE (NE, NE)	69.1 (61.2, 76.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	19 (18.6)	29 (15.0)
Number of Subjects Censored, n (%)	83 (81.4)	164 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.91, NE)	9.20 (9.00, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.542 (0.311)
95% CI		(0.294, 0.998)
Log-rank p-value		0.055

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.7 (74.0, 89.4)	88.7 (84.2, 93.3)
6 months	76.2 (63.7, 88.8)	84.0 (78.1, 90.0)
9 months	NE (NE, NE)	82.6 (76.2, 89.1)
12 months	NE (NE, NE)	74.1 (61.6, 86.7)
18 months	NE (NE, NE)	74.1 (61.6, 86.7)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	15 (14.7)	41 (21.2)
Number of Subjects Censored, n (%)	87 (85.3)	152 (78.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.57, NE)	6.41 (3.71, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.143 (0.311)
95% CI		(0.622, 2.102)
Log-rank p-value		0.557

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.6 (78.7, 92.6)	83.9 (78.5, 89.2)
6 months	80.3 (68.2, 92.4)	78.9 (72.5, 85.2)
9 months	NE (NE, NE)	72.5 (64.0, 81.0)
12 months	NE (NE, NE)	68.0 (56.2, 79.7)
18 months	NE (NE, NE)	68.0 (56.2, 79.7)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	8 (7.8)	38 (19.7)
Number of Subjects Censored, n (%)	94 (92.2)	155 (80.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	7.10 (3.75, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.070 (0.394)
95% CI		(0.956, 4.484)
Log-rank p-value		0.061

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.9 (86.5, 97.3)	83.6 (78.2, 89.0)
6 months	91.9 (86.5, 97.3)	78.0 (71.3, 84.7)
9 months	NE (NE, NE)	74.2 (66.0, 82.4)
12 months	NE (NE, NE)	74.2 (66.0, 82.4)
18 months	NE (NE, NE)	74.2 (66.0, 82.4)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	9 (8.8)	29 (15.0)
Number of Subjects Censored, n (%)	93 (91.2)	164 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	10.18 (7.10, NE)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.4, 8.4*	0.1, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.112 (0.400)
95% CI		(0.508, 2.434)
Log-rank p-value		0.820

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.8 (85.1, 96.6)	90.9 (86.8, 95.0)
6 months	90.8 (85.1, 96.6)	85.5 (79.7, 91.3)
9 months	NE (NE, NE)	80.2 (72.2, 88.2)
12 months	NE (NE, NE)	70.7 (56.4, 85.0)
18 months	NE (NE, NE)	70.7 (56.4, 85.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	3 (2.9)	29 (15.0)
Number of Subjects Censored, n (%)	99 (97.1)	164 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.87, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.258 (0.611)
95% CI		(1.589, 17.397)
Log-rank p-value		0.004

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (93.5, 100.0)	86.9 (82.1, 91.7)
6 months	96.9 (93.5, 100.0)	84.1 (78.6, 89.7)
9 months	NE (NE, NE)	82.3 (75.8, 88.8)
12 months	NE (NE, NE)	82.3 (75.8, 88.8)
18 months	NE (NE, NE)	82.3 (75.8, 88.8)
Median Follow-up Time (months)	2.83	4.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	2 (2.0)	18 (9.3)
Number of Subjects Censored, n (%)	100 (98.0)	175 (90.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.998 (0.752)
95% CI		(0.916, 17.457)
Log-rank p-value		0.049

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (95.3, 100.0)	93.1 (89.5, 96.7)
6 months	98.0 (95.3, 100.0)	89.2 (84.4, 94.0)
9 months	NE (NE, NE)	89.2 (84.4, 94.0)
12 months	NE (NE, NE)	89.2 (84.4, 94.0)
18 months	NE (NE, NE)	89.2 (84.4, 94.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	1 (1.0)	5 (2.6)
Number of Subjects Censored, n (%)	101 (99.0)	188 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.8*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.449 (1.157)
95% CI		(0.150, 13.984)
Log-rank p-value		0.703

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.0, 100.0)	98.9 (97.5, 100.0)
6 months	99.0 (97.0, 100.0)	96.9 (93.7, 100.0)
9 months	NE (NE, NE)	94.7 (89.3, 100.0)
12 months	NE (NE, NE)	94.7 (89.3, 100.0)
18 months	NE (NE, NE)	94.7 (89.3, 100.0)
Median Follow-up Time (months)	2.83	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	0	2 (1.0)
Number of Subjects Censored, n (%)	102 (100.0)	191 (99.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.351

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.9 (97.5, 100.0)
6 months	100.0 (100.0, 100.0)	98.9 (97.5, 100.0)
9 months	NE (NE, NE)	98.9 (97.5, 100.0)
12 months	NE (NE, NE)	98.9 (97.5, 100.0)
18 months	NE (NE, NE)	98.9 (97.5, 100.0)
Median Follow-up Time (months)	2.83	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	5 (4.9)	1 (0.5)
Number of Subjects Censored, n (%)	97 (95.1)	192 (99.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 8.4*	0.8*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.032 (1.456)
95% CI		(0.002, 0.548)
Log-rank p-value		0.004

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (90.5, 99.3)	100.0 (100.0, 100.0)
6 months	94.9 (90.5, 99.3)	98.8 (96.3, 100.0)
9 months	NE (NE, NE)	98.8 (96.3, 100.0)
12 months	NE (NE, NE)	98.8 (96.3, 100.0)
18 months	NE (NE, NE)	98.8 (96.3, 100.0)
Median Follow-up Time (months)	2.83	4.93

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	17 (16.7)	80 (41.5)
Number of Subjects Censored, n (%)	85 (83.3)	113 (58.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.27, NE)	1.64 (0.95, 2.00)
Median (95% CI)	NE (NE, NE)	9.43 (5.68, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.5*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.210 (0.272)
95% CI		(1.297, 3.767)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.9 (76.6, 91.1)	65.6 (58.8, 72.4)
6 months	77.9 (64.7, 91.1)	57.2 (49.4, 64.9)
9 months	NE (NE, NE)	51.3 (42.2, 60.3)
12 months	NE (NE, NE)	45.6 (32.3, 58.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	11 (10.8)	46 (23.8)
Number of Subjects Censored, n (%)	91 (89.2)	147 (76.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.27, NE)	6.44 (2.86, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.909 (0.343)
95% CI		(0.975, 3.739)
Log-rank p-value		0.053

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.7 (83.7, 95.8)	79.8 (74.0, 85.5)
6 months	84.1 (72.0, 96.2)	76.5 (70.2, 82.9)
9 months	NE (NE, NE)	72.2 (64.4, 79.9)
12 months	NE (NE, NE)	67.7 (56.4, 78.9)
18 months	NE (NE, NE)	67.7 (56.4, 78.9)
Median Follow-up Time (months)	2.83	4.47

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	0	9 (4.7)
Number of Subjects Censored, n (%)	102 (100.0)	184 (95.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.040

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.6 (92.6, 98.6)
6 months	100.0 (100.0, 100.0)	95.6 (92.6, 98.6)
9 months	NE (NE, NE)	93.3 (88.0, 98.6)
12 months	NE (NE, NE)	93.3 (88.0, 98.6)
18 months	NE (NE, NE)	93.3 (88.0, 98.6)
Median Follow-up Time (months)	2.83	4.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	2 (2.0)	2 (1.0)
Number of Subjects Censored, n (%)	100 (98.0)	191 (99.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.8*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.197 (1.109)
95% CI		(0.022, 1.732)
Log-rank p-value		0.097

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (95.3, 100.0)	100.0 (100.0, 100.0)
6 months	98.0 (95.3, 100.0)	97.9 (95.0, 100.0)
9 months	NE (NE, NE)	97.9 (95.0, 100.0)
12 months	NE (NE, NE)	97.9 (95.0, 100.0)
18 months	NE (NE, NE)	97.9 (95.0, 100.0)
Median Follow-up Time (months)	2.83	4.93

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	1 (1.0)	5 (2.6)
Number of Subjects Censored, n (%)	101 (99.0)	188 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.305 (1.104)
95% CI		(0.265, 20.057)
Log-rank p-value		0.364

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.0, 100.0)	97.9 (95.9, 99.9)
6 months	99.0 (97.0, 100.0)	97.1 (94.6, 99.6)
9 months	NE (NE, NE)	97.1 (94.6, 99.6)
12 months	NE (NE, NE)	97.1 (94.6, 99.6)
18 months	NE (NE, NE)	97.1 (94.6, 99.6)
Median Follow-up Time (months)	2.83	4.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	0	3 (1.6)
Number of Subjects Censored, n (%)	102 (100.0)	190 (98.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.8*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.316

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.9 (97.4, 100.0)
6 months	100.0 (100.0, 100.0)	97.7 (95.0, 100.0)
9 months	NE (NE, NE)	97.7 (95.0, 100.0)
12 months	NE (NE, NE)	97.7 (95.0, 100.0)
18 months	NE (NE, NE)	97.7 (95.0, 100.0)
Median Follow-up Time (months)	2.83	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	0	8 (4.1)
Number of Subjects Censored, n (%)	102 (100.0)	185 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.100

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.4 (95.1, 99.6)
6 months	100.0 (100.0, 100.0)	95.3 (91.6, 99.0)
9 months	NE (NE, NE)	93.3 (88.0, 98.6)
12 months	NE (NE, NE)	93.3 (88.0, 98.6)
18 months	NE (NE, NE)	93.3 (88.0, 98.6)
Median Follow-up Time (months)	2.83	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	1 (1.0)	4 (2.1)
Number of Subjects Censored, n (%)	101 (99.0)	189 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.009 (1.124)
95% CI		(0.222, 18.167)
Log-rank p-value		0.522

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.1, 100.0)	97.8 (95.7, 99.9)
6 months	99.0 (97.1, 100.0)	97.8 (95.7, 99.9)
9 months	NE (NE, NE)	97.8 (95.7, 99.9)
12 months	NE (NE, NE)	97.8 (95.7, 99.9)
18 months	NE (NE, NE)	97.8 (95.7, 99.9)
Median Follow-up Time (months)	2.83	4.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	1 (1.0)	9 (4.7)
Number of Subjects Censored, n (%)	101 (99.0)	184 (95.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.824 (1.057)
95% CI		(0.608, 38.266)
Log-rank p-value		0.091

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.0, 100.0)	95.7 (92.9, 98.6)
6 months	99.0 (97.0, 100.0)	95.0 (91.9, 98.2)
9 months	NE (NE, NE)	95.0 (91.9, 98.2)
12 months	NE (NE, NE)	95.0 (91.9, 98.2)
18 months	NE (NE, NE)	95.0 (91.9, 98.2)
Median Follow-up Time (months)	2.83	4.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	2 (2.0)	6 (3.1)
Number of Subjects Censored, n (%)	100 (98.0)	187 (96.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.515 (0.823)
95% CI		(0.302, 7.608)
Log-rank p-value		0.636

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (95.3, 100.0)	96.9 (94.4, 99.3)
6 months	98.0 (95.3, 100.0)	96.9 (94.4, 99.3)
9 months	NE (NE, NE)	96.9 (94.4, 99.3)
12 months	NE (NE, NE)	96.9 (94.4, 99.3)
18 months	NE (NE, NE)	96.9 (94.4, 99.3)
Median Follow-up Time (months)	2.83	4.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	1 (1.0)	5 (2.6)
Number of Subjects Censored, n (%)	101 (99.0)	188 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.526 (1.146)
95% CI		(0.162, 14.421)
Log-rank p-value		0.719

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.0, 100.0)	99.0 (97.5, 100.0)
6 months	99.0 (97.0, 100.0)	96.0 (92.4, 99.6)
9 months	NE (NE, NE)	96.0 (92.4, 99.6)
12 months	NE (NE, NE)	96.0 (92.4, 99.6)
18 months	NE (NE, NE)	96.0 (92.4, 99.6)
Median Follow-up Time (months)	2.83	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	20 (19.6)	79 (40.9)
Number of Subjects Censored, n (%)	82 (80.4)	114 (59.1)
Time to first TEAE (months)		
25% percentile (95% CI)	5.82 (1.64, NE)	1.81 (1.48, 2.79)
Median (95% CI)	NE (5.82, NE)	7.16 (5.78, NE)
75% percentile (95% CI)	NE (5.82, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.685 (0.256)
95% CI		(1.020, 2.783)
Log-rank p-value		0.034

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.9 (74.3, 89.5)	66.7 (59.9, 73.4)
6 months	51.6 (9.6, 93.5)	56.3 (48.2, 64.4)
9 months	NE (NE, NE)	48.3 (38.6, 58.0)
12 months	NE (NE, NE)	48.3 (38.6, 58.0)
18 months	NE (NE, NE)	48.3 (38.6, 58.0)
Median Follow-up Time (months)	2.83	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	6 (5.9)	20 (10.4)
Number of Subjects Censored, n (%)	96 (94.1)	173 (89.6)
Time to first TEAE (months)		
25% percentile (95% CI)	5.82 (5.82, NE)	NE (NE, NE)
Median (95% CI)	NE (5.82, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (5.82, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.234 (0.483)
95% CI		(0.479, 3.179)
Log-rank p-value		0.661

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (89.7, 99.2)	92.3 (88.5, 96.2)
6 months	70.8 (30.6, 100.0)	88.3 (82.9, 93.7)
9 months	NE (NE, NE)	85.1 (78.4, 91.9)
12 months	NE (NE, NE)	85.1 (78.4, 91.9)
18 months	NE (NE, NE)	85.1 (78.4, 91.9)
Median Follow-up Time (months)	2.83	4.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	2 (2.0)	17 (8.8)
Number of Subjects Censored, n (%)	100 (98.0)	176 (91.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.970 (0.765)
95% CI		(0.663, 13.301)
Log-rank p-value		0.139

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (95.3, 100.0)	94.0 (90.6, 97.5)
6 months	98.0 (95.3, 100.0)	90.1 (85.0, 95.2)
9 months	NE (NE, NE)	87.0 (80.6, 93.5)
12 months	NE (NE, NE)	87.0 (80.6, 93.5)
18 months	NE (NE, NE)	87.0 (80.6, 93.5)
Median Follow-up Time (months)	2.83	4.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	2 (2.0)	17 (8.8)
Number of Subjects Censored, n (%)	100 (98.0)	176 (91.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.908 (0.768)
95% CI		(0.646, 13.097)
Log-rank p-value		0.147

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (95.3, 100.0)	94.7 (91.5, 97.9)
6 months	98.0 (95.3, 100.0)	91.1 (86.4, 95.8)
9 months	NE (NE, NE)	86.6 (79.9, 93.3)
12 months	NE (NE, NE)	86.6 (79.9, 93.3)
18 months	NE (NE, NE)	86.6 (79.9, 93.3)
Median Follow-up Time (months)	2.83	4.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	3 (2.9)	17 (8.8)
Number of Subjects Censored, n (%)	99 (97.1)	176 (91.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.091 (0.642)
95% CI		(0.594, 7.360)
Log-rank p-value		0.274

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.0 (93.7, 100.0)	94.7 (91.6, 97.9)
6 months	97.0 (93.7, 100.0)	90.6 (85.9, 95.3)
9 months	NE (NE, NE)	87.1 (80.6, 93.6)
12 months	NE (NE, NE)	87.1 (80.6, 93.6)
18 months	NE (NE, NE)	87.1 (80.6, 93.6)
Median Follow-up Time (months)	2.83	4.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	2 (2.0)	13 (6.7)
Number of Subjects Censored, n (%)	100 (98.0)	180 (93.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.407 (0.773)
95% CI		(0.529, 10.945)
Log-rank p-value		0.228

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.0, 100.0)	94.6 (91.4, 97.9)
6 months	94.7 (86.2, 100.0)	93.6 (89.9, 97.4)
9 months	NE (NE, NE)	89.0 (81.3, 96.7)
12 months	NE (NE, NE)	89.0 (81.3, 96.7)
18 months	NE (NE, NE)	89.0 (81.3, 96.7)
Median Follow-up Time (months)	2.83	4.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	3 (2.9)	9 (4.7)
Number of Subjects Censored, n (%)	99 (97.1)	184 (95.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.069 (0.695)
95% CI		(0.274, 4.176)
Log-rank p-value		0.978

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.6 (92.9, 100.0)	96.2 (93.4, 99.0)
6 months	96.6 (92.9, 100.0)	95.0 (91.4, 98.6)
9 months	NE (NE, NE)	93.6 (89.1, 98.1)
12 months	NE (NE, NE)	93.6 (89.1, 98.1)
18 months	NE (NE, NE)	93.6 (89.1, 98.1)
Median Follow-up Time (months)	2.83	4.93

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	1 (1.0)	12 (6.2)
Number of Subjects Censored, n (%)	101 (99.0)	181 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.331 (1.047)
95% CI		(0.685, 41.493)
Log-rank p-value		0.082

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.1, 100.0)	94.0 (90.5, 97.4)
6 months	99.0 (97.1, 100.0)	93.2 (89.4, 96.9)
9 months	NE (NE, NE)	93.2 (89.4, 96.9)
12 months	NE (NE, NE)	93.2 (89.4, 96.9)
18 months	NE (NE, NE)	93.2 (89.4, 96.9)
Median Follow-up Time (months)	2.83	4.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	1 (1.0)	6 (3.1)
Number of Subjects Censored, n (%)	101 (99.0)	187 (96.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.086 (1.108)
95% CI		(0.238, 18.301)
Log-rank p-value		0.455

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.0, 100.0)	97.7 (95.5, 99.9)
6 months	99.0 (97.0, 100.0)	96.8 (94.0, 99.6)
9 months	NE (NE, NE)	95.5 (91.7, 99.3)
12 months	NE (NE, NE)	95.5 (91.7, 99.3)
18 months	NE (NE, NE)	95.5 (91.7, 99.3)
Median Follow-up Time (months)	2.83	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	1 (1.0)	5 (2.6)
Number of Subjects Censored, n (%)	101 (99.0)	188 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.8*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.114 (1.116)
95% CI		(0.237, 18.854)
Log-rank p-value		0.509

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.0, 100.0)	97.9 (95.9, 99.9)
6 months	99.0 (97.0, 100.0)	97.9 (95.9, 99.9)
9 months	NE (NE, NE)	96.0 (91.8, 100.0)
12 months	NE (NE, NE)	96.0 (91.8, 100.0)
18 months	NE (NE, NE)	96.0 (91.8, 100.0)
Median Follow-up Time (months)	2.83	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	1 (1.0)	5 (2.6)
Number of Subjects Censored, n (%)	101 (99.0)	188 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.8*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.102 (1.117)
95% CI		(0.235, 18.769)
Log-rank p-value		0.512

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.0, 100.0)	97.9 (95.8, 99.9)
6 months	99.0 (97.0, 100.0)	97.9 (95.8, 99.9)
9 months	NE (NE, NE)	96.0 (91.8, 100.0)
12 months	NE (NE, NE)	96.0 (91.8, 100.0)
18 months	NE (NE, NE)	96.0 (91.8, 100.0)
Median Follow-up Time (months)	2.83	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	29 (28.4)	78 (40.4)
Number of Subjects Censored, n (%)	73 (71.6)	115 (59.6)
Time to first TEAE (months)		
25% percentile (95% CI)	1.81 (0.69, NE)	0.69 (0.69, 1.38)
Median (95% CI)	NE (NE, NE)	11.53 (6.41, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.382 (0.221)
95% CI		(0.896, 2.132)
Log-rank p-value		0.148

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	70.5 (61.4, 79.6)	63.6 (56.8, 70.4)
6 months	70.5 (61.4, 79.6)	61.2 (54.1, 68.3)
9 months	NE (NE, NE)	55.5 (47.1, 63.9)
12 months	NE (NE, NE)	46.2 (28.3, 64.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.78	2.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	9 (8.8)	42 (21.8)
Number of Subjects Censored, n (%)	93 (91.2)	151 (78.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.61, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.625 (0.369)
95% CI		(1.274, 5.408)
Log-rank p-value		0.007

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.7 (84.9, 96.5)	78.0 (72.2, 83.9)
6 months	90.7 (84.9, 96.5)	78.0 (72.2, 83.9)
9 months	NE (NE, NE)	78.0 (72.2, 83.9)
12 months	NE (NE, NE)	78.0 (72.2, 83.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	8 (7.8)	19 (9.8)
Number of Subjects Censored, n (%)	94 (92.2)	174 (90.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	14.32 (10.28, NE)
Median (95% CI)	NE (NE, NE)	NE (14.32, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (14.32, NE)
Min, Max	0.0, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.993 (0.439)
95% CI		(0.420, 2.347)
Log-rank p-value		0.999

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.0 (86.8, 97.3)	92.6 (88.8, 96.3)
6 months	92.0 (86.8, 97.3)	91.9 (88.0, 95.8)
9 months	NE (NE, NE)	89.3 (84.0, 94.5)
12 months	NE (NE, NE)	83.3 (71.0, 95.6)
18 months	NE (NE, NE)	55.6 (10.4, 100.0)
Median Follow-up Time (months)	2.83	4.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	14 (13.7)	19 (9.8)
Number of Subjects Censored, n (%)	88 (86.3)	174 (90.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.613 (0.363)
95% CI		(0.301, 1.247)
Log-rank p-value		0.207

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.8 (78.8, 92.7)	91.1 (87.1, 95.1)
6 months	85.8 (78.8, 92.7)	91.1 (87.1, 95.1)
9 months	NE (NE, NE)	89.7 (84.9, 94.5)
12 months	NE (NE, NE)	79.7 (60.8, 98.7)
18 months	NE (NE, NE)	79.7 (60.8, 98.7)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	1 (1.0)	8 (4.1)
Number of Subjects Censored, n (%)	101 (99.0)	185 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.699 (1.065)
95% CI		(0.459, 29.808)
Log-rank p-value		0.206

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.1, 100.0)	95.8 (92.9, 98.6)
6 months	99.0 (97.1, 100.0)	95.8 (92.9, 98.6)
9 months	NE (NE, NE)	95.8 (92.9, 98.6)
12 months	NE (NE, NE)	95.8 (92.9, 98.6)
18 months	NE (NE, NE)	95.8 (92.9, 98.6)
Median Follow-up Time (months)	2.83	4.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	0	4 (2.1)
Number of Subjects Censored, n (%)	102 (100.0)	189 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.252

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.0 (97.5, 100.0)
6 months	100.0 (100.0, 100.0)	98.0 (95.5, 100.0)
9 months	NE (NE, NE)	96.6 (92.9, 100.0)
12 months	NE (NE, NE)	96.6 (92.9, 100.0)
18 months	NE (NE, NE)	96.6 (92.9, 100.0)
Median Follow-up Time (months)	2.83	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Vascular disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	11 (10.8)	90 (46.6)
Number of Subjects Censored, n (%)	91 (89.2)	103 (53.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.69 (0.66, 0.95)
Median (95% CI)	NE (NE, NE)	7.39 (2.56, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.056 (0.321)
95% CI		(2.696, 9.481)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Vascular disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.6 (82.2, 95.0)	54.4 (47.3, 61.6)
6 months	88.6 (82.2, 95.0)	52.8 (45.5, 60.1)
9 months	NE (NE, NE)	48.7 (40.1, 57.4)
12 months	NE (NE, NE)	48.7 (40.1, 57.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	9 (8.8)	87 (45.1)
Number of Subjects Censored, n (%)	93 (91.2)	106 (54.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.69 (0.69, 1.05)
Median (95% CI)	NE (NE, NE)	7.39 (2.79, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.998 (0.352)
95% CI		(3.010, 11.952)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.6 (84.7, 96.5)	56.7 (49.6, 63.8)
6 months	90.6 (84.7, 96.5)	55.1 (47.8, 62.3)
9 months	NE (NE, NE)	49.2 (40.1, 58.2)
12 months	NE (NE, NE)	49.2 (40.1, 58.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	22 (21.6)	73 (37.8)
Number of Subjects Censored, n (%)	80 (78.4)	120 (62.2)
Time to first TEAE (months)		
25% percentile (95% CI)	3.71 (1.64, NE)	1.68 (1.15, 2.53)
Median (95% CI)	NE (NE, NE)	9.76 (7.20, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.619 (0.249)
95% CI		(0.994, 2.637)
Log-rank p-value		0.040

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.6 (71.6, 87.6)	66.6 (59.8, 73.3)
6 months	70.2 (56.1, 84.3)	60.8 (53.1, 68.4)
9 months	NE (NE, NE)	53.2 (42.1, 64.3)
12 months	NE (NE, NE)	48.8 (35.6, 61.9)
18 months	NE (NE, NE)	48.8 (35.6, 61.9)
Median Follow-up Time (months)	2.83	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	7 (6.9)	21 (10.9)
Number of Subjects Censored, n (%)	95 (93.1)	172 (89.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.293 (0.445)
95% CI		(0.540, 3.096)
Log-rank p-value		0.496

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (87.8, 98.0)	90.2 (85.9, 94.5)
6 months	92.9 (87.8, 98.0)	88.3 (83.3, 93.3)
9 months	NE (NE, NE)	87.0 (81.5, 92.5)
12 months	NE (NE, NE)	87.0 (81.5, 92.5)
18 months	NE (NE, NE)	87.0 (81.5, 92.5)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	5 (4.9)	24 (12.4)
Number of Subjects Censored, n (%)	97 (95.1)	169 (87.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.20, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.377 (0.499)
95% CI		(0.894, 6.320)
Log-rank p-value		0.081

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.0 (90.7, 99.3)	89.4 (85.0, 93.8)
6 months	95.0 (90.7, 99.3)	87.5 (82.4, 92.6)
9 months	NE (NE, NE)	83.6 (76.5, 90.8)
12 months	NE (NE, NE)	83.6 (76.5, 90.8)
18 months	NE (NE, NE)	83.6 (76.5, 90.8)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	3 (2.9)	10 (5.2)
Number of Subjects Censored, n (%)	99 (97.1)	183 (94.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.424 (0.668)
95% CI		(0.384, 5.280)
Log-rank p-value		0.449

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.8, 100.0)	95.2 (92.2, 98.3)
6 months	89.9 (77.9, 100.0)	94.1 (90.4, 97.8)
9 months	NE (NE, NE)	94.1 (90.4, 97.8)
12 months	NE (NE, NE)	94.1 (90.4, 97.8)
18 months	NE (NE, NE)	94.1 (90.4, 97.8)
Median Follow-up Time (months)	2.83	4.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	3 (2.9)	7 (3.6)
Number of Subjects Censored, n (%)	99 (97.1)	186 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.159 (0.704)
95% CI		(0.291, 4.605)
Log-rank p-value		0.854

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.0 (93.6, 100.0)	96.8 (94.3, 99.3)
6 months	97.0 (93.6, 100.0)	95.5 (92.0, 99.0)
9 months	NE (NE, NE)	95.5 (92.0, 99.0)
12 months	NE (NE, NE)	95.5 (92.0, 99.0)
18 months	NE (NE, NE)	95.5 (92.0, 99.0)
Median Follow-up Time (months)	2.83	4.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	1 (1.0)	7 (3.6)
Number of Subjects Censored, n (%)	101 (99.0)	186 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.244 (1.115)
95% CI		(0.252, 19.939)
Log-rank p-value		0.393

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.0, 100.0)	97.9 (95.8, 99.9)
6 months	99.0 (97.0, 100.0)	97.9 (95.8, 99.9)
9 months	NE (NE, NE)	90.1 (80.8, 99.3)
12 months	NE (NE, NE)	90.1 (80.8, 99.3)
18 months	NE (NE, NE)	90.1 (80.8, 99.3)
Median Follow-up Time (months)	2.83	4.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	0	7 (3.6)
Number of Subjects Censored, n (%)	102 (100.0)	186 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.8*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.061

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.2 (93.5, 99.0)
6 months	100.0 (100.0, 100.0)	96.2 (93.5, 99.0)
9 months	NE (NE, NE)	96.2 (93.5, 99.0)
12 months	NE (NE, NE)	96.2 (93.5, 99.0)
18 months	NE (NE, NE)	96.2 (93.5, 99.0)
Median Follow-up Time (months)	2.83	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	13 (12.7)	85 (44.0)
Number of Subjects Censored, n (%)	89 (87.3)	108 (56.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	0.72 (0.66, 1.35)
Median (95% CI)	NE (NE, NE)	13.14 (3.58, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.14, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.809 (0.300)
95% CI		(2.117, 6.852)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.1 (81.7, 94.4)	58.5 (51.5, 65.6)
6 months	83.4 (72.8, 94.1)	54.1 (46.6, 61.6)
9 months	NE (NE, NE)	54.1 (46.6, 61.6)
12 months	NE (NE, NE)	54.1 (46.6, 61.6)
18 months	NE (NE, NE)	27.0 (0.0, 64.7)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	4 (3.9)	53 (27.5)
Number of Subjects Censored, n (%)	98 (96.1)	140 (72.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	2.50 (1.51, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		7.547 (0.520)
95% CI		(2.722, 20.927)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.0 (92.2, 99.8)	74.8 (68.6, 81.0)
6 months	96.0 (92.2, 99.8)	70.0 (62.9, 77.1)
9 months	NE (NE, NE)	70.0 (62.9, 77.1)
12 months	NE (NE, NE)	70.0 (62.9, 77.1)
18 months	NE (NE, NE)	70.0 (62.9, 77.1)
Median Follow-up Time (months)	2.83	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	2 (2.0)	9 (4.7)
Number of Subjects Censored, n (%)	100 (98.0)	184 (95.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.004 (0.789)
95% CI		(0.427, 9.415)
Log-rank p-value		0.344

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (95.3, 100.0)	95.1 (92.0, 98.3)
6 months	98.0 (95.3, 100.0)	95.1 (92.0, 98.3)
9 months	NE (NE, NE)	95.1 (92.0, 98.3)
12 months	NE (NE, NE)	95.1 (92.0, 98.3)
18 months	NE (NE, NE)	95.1 (92.0, 98.3)
Median Follow-up Time (months)	2.83	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	3 (2.9)	6 (3.1)
Number of Subjects Censored, n (%)	99 (97.1)	187 (96.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.957 (0.716)
95% CI		(0.235, 3.897)
Log-rank p-value		0.908

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (95.2, 100.0)	96.8 (94.4, 99.3)
6 months	93.5 (84.6, 100.0)	96.8 (94.4, 99.3)
9 months	NE (NE, NE)	96.8 (94.4, 99.3)
12 months	NE (NE, NE)	96.8 (94.4, 99.3)
18 months	NE (NE, NE)	96.8 (94.4, 99.3)
Median Follow-up Time (months)	2.83	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Nervous system disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	18 (17.6)	44 (22.8)
Number of Subjects Censored, n (%)	84 (82.4)	149 (77.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.91, NE)	5.49 (2.56, NE)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.163 (0.285)
95% CI		(0.665, 2.033)
Log-rank p-value		0.675

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Nervous system disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.5 (73.7, 89.3)	81.2 (75.6, 86.7)
6 months	81.5 (73.7, 89.3)	74.7 (67.7, 81.6)
9 months	NE (NE, NE)	74.7 (67.7, 81.6)
12 months	NE (NE, NE)	74.7 (67.7, 81.6)
18 months	NE (NE, NE)	74.7 (67.7, 81.6)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	8 (7.8)	18 (9.3)
Number of Subjects Censored, n (%)	94 (92.2)	175 (90.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.1, 8.4*	0.0, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.046 (0.433)
95% CI		(0.447, 2.445)
Log-rank p-value		0.935

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.7 (86.1, 97.2)	92.2 (88.4, 96.0)
6 months	91.7 (86.1, 97.2)	90.3 (85.9, 94.8)
9 months	NE (NE, NE)	90.3 (85.9, 94.8)
12 months	NE (NE, NE)	90.3 (85.9, 94.8)
18 months	NE (NE, NE)	90.3 (85.9, 94.8)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	2 (2.0)	4 (2.1)
Number of Subjects Censored, n (%)	100 (98.0)	189 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.994 (0.876)
95% CI		(0.179, 5.530)
Log-rank p-value		0.972

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (95.3, 100.0)	97.9 (95.9, 99.9)
6 months	98.0 (95.3, 100.0)	97.9 (95.9, 99.9)
9 months	NE (NE, NE)	97.9 (95.9, 99.9)
12 months	NE (NE, NE)	97.9 (95.9, 99.9)
18 months	NE (NE, NE)	97.9 (95.9, 99.9)
Median Follow-up Time (months)	2.83	4.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	3 (2.9)	3 (1.6)
Number of Subjects Censored, n (%)	99 (97.1)	190 (98.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.616 (0.817)
95% CI		(0.124, 3.056)
Log-rank p-value		0.547

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.0 (93.6, 100.0)	98.4 (96.7, 100.0)
6 months	97.0 (93.6, 100.0)	98.4 (96.7, 100.0)
9 months	NE (NE, NE)	98.4 (96.7, 100.0)
12 months	NE (NE, NE)	98.4 (96.7, 100.0)
18 months	NE (NE, NE)	98.4 (96.7, 100.0)
Median Follow-up Time (months)	2.83	4.93

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	11 (10.8)	44 (22.8)
Number of Subjects Censored, n (%)	91 (89.2)	149 (77.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	6.47 (3.35, 13.60)
Median (95% CI)	NE (NE, NE)	13.60 (11.96, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.0, 8.4*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.775 (0.348)
95% CI		(0.898, 3.508)
Log-rank p-value		0.140

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.7 (83.7, 95.8)	82.3 (76.8, 87.8)
6 months	85.0 (74.3, 95.7)	75.6 (68.7, 82.4)
9 months	NE (NE, NE)	74.1 (66.8, 81.4)
12 months	NE (NE, NE)	63.5 (43.3, 83.7)
18 months	NE (NE, NE)	42.3 (5.9, 78.8)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	5 (4.9)	38 (19.7)
Number of Subjects Censored, n (%)	97 (95.1)	155 (80.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.60 (3.68, NE)
Median (95% CI)	NE (NE, NE)	NE (13.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.4*, 8.4*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.830 (0.484)
95% CI		(1.483, 9.892)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (90.6, 99.3)	83.9 (78.6, 89.2)
6 months	94.9 (90.6, 99.3)	78.0 (71.5, 84.6)
9 months	NE (NE, NE)	78.0 (71.5, 84.6)
12 months	NE (NE, NE)	78.0 (71.5, 84.6)
18 months	NE (NE, NE)	52.0 (10.2, 93.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	0	4 (2.1)
Number of Subjects Censored, n (%)	102 (100.0)	189 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.8*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.167

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.4 (96.6, 100.0)
6 months	100.0 (100.0, 100.0)	97.6 (95.3, 100.0)
9 months	NE (NE, NE)	97.6 (95.3, 100.0)
12 months	NE (NE, NE)	97.6 (95.3, 100.0)
18 months	NE (NE, NE)	97.6 (95.3, 100.0)
Median Follow-up Time (months)	2.83	4.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Infections and infestations**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	13 (12.7)	48 (24.9)
Number of Subjects Censored, n (%)	89 (87.3)	145 (75.1)
Time to first TEAE (months)		
25% percentile (95% CI)	5.78 (3.71, NE)	5.78 (3.58, 6.83)
Median (95% CI)	NE (5.78, NE)	NE (11.53, NE)
75% percentile (95% CI)	NE (5.78, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.148 (0.329)
95% CI		(0.602, 2.190)
Log-rank p-value		0.642

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Infections and infestations**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.6 (83.5, 95.7)	85.0 (79.8, 90.1)
6 months	51.1 (8.5, 93.7)	72.9 (65.2, 80.6)
9 months	NE (NE, NE)	62.3 (51.9, 72.8)
12 months	NE (NE, NE)	54.5 (37.6, 71.5)
18 months	NE (NE, NE)	54.5 (37.6, 71.5)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	4 (3.9)	7 (3.6)
Number of Subjects Censored, n (%)	98 (96.1)	186 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.14, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.442 (0.688)
95% CI		(0.115, 1.702)
Log-rank p-value		0.291

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.1, 100.0)	97.9 (95.8, 99.9)
6 months	83.2 (66.5, 99.9)	96.7 (93.6, 99.8)
9 months	NE (NE, NE)	93.9 (89.0, 98.7)
12 months	NE (NE, NE)	93.9 (89.0, 98.7)
18 months	NE (NE, NE)	93.9 (89.0, 98.7)
Median Follow-up Time (months)	2.83	4.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	3 (2.9)	6 (3.1)
Number of Subjects Censored, n (%)	99 (97.1)	187 (96.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (11.56, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.8*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.355 (0.801)
95% CI		(0.074, 1.708)
Log-rank p-value		0.209

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (94.8, 100.0)	99.4 (98.4, 100.0)
6 months	91.7 (79.8, 100.0)	96.9 (93.9, 99.9)
9 months	NE (NE, NE)	95.3 (91.1, 99.6)
12 months	NE (NE, NE)	85.8 (67.7, 100.0)
18 months	NE (NE, NE)	85.8 (67.7, 100.0)
Median Follow-up Time (months)	2.83	4.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	0	3 (1.6)
Number of Subjects Censored, n (%)	102 (100.0)	190 (98.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.8*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.353

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.8 (97.2, 100.0)
6 months	100.0 (100.0, 100.0)	97.6 (94.8, 100.0)
9 months	NE (NE, NE)	97.6 (94.8, 100.0)
12 months	NE (NE, NE)	97.6 (94.8, 100.0)
18 months	NE (NE, NE)	97.6 (94.8, 100.0)
Median Follow-up Time (months)	2.83	4.93

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	9 (8.8)	31 (16.1)
Number of Subjects Censored, n (%)	93 (91.2)	162 (83.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.85, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.501 (0.387)
95% CI		(0.703, 3.203)
Log-rank p-value		0.293

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.4 (84.4, 96.4)	87.1 (82.3, 91.9)
6 months	90.4 (84.4, 96.4)	81.1 (74.5, 87.7)
9 months	NE (NE, NE)	79.7 (72.6, 86.7)
12 months	NE (NE, NE)	79.7 (72.6, 86.7)
18 months	NE (NE, NE)	79.7 (72.6, 86.7)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	8 (7.8)	17 (8.8)
Number of Subjects Censored, n (%)	94 (92.2)	176 (91.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.729 (0.450)
95% CI		(0.301, 1.762)
Log-rank p-value		0.480

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.4 (85.6, 97.2)	94.6 (91.4, 97.9)
6 months	91.4 (85.6, 97.2)	88.6 (82.9, 94.3)
9 months	NE (NE, NE)	87.2 (81.0, 93.4)
12 months	NE (NE, NE)	87.2 (81.0, 93.4)
18 months	NE (NE, NE)	87.2 (81.0, 93.4)
Median Follow-up Time (months)	2.83	4.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	0	12 (6.2)
Number of Subjects Censored, n (%)	102 (100.0)	181 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.7, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.013

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.5 (90.0, 97.1)
6 months	100.0 (100.0, 100.0)	93.5 (90.0, 97.1)
9 months	NE (NE, NE)	93.5 (90.0, 97.1)
12 months	NE (NE, NE)	93.5 (90.0, 97.1)
18 months	NE (NE, NE)	93.5 (90.0, 97.1)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Endocrine disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	0	43 (22.3)
Number of Subjects Censored, n (%)	102 (100.0)	150 (77.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.75 (3.84, NE)
Median (95% CI)	NE (NE, NE)	NE (9.33, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Endocrine disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	85.5 (80.4, 90.6)
6 months	100.0 (100.0, 100.0)	72.7 (64.7, 80.6)
9 months	NE (NE, NE)	69.1 (60.2, 78.1)
12 months	NE (NE, NE)	63.8 (50.8, 76.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	0	42 (21.8)
Number of Subjects Censored, n (%)	102 (100.0)	151 (78.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.78 (3.91, 9.33)
Median (95% CI)	NE (NE, NE)	NE (9.33, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	86.0 (81.0, 91.0)
6 months	100.0 (100.0, 100.0)	74.2 (66.5, 81.9)
9 months	NE (NE, NE)	68.5 (59.0, 78.0)
12 months	NE (NE, NE)	63.2 (50.0, 76.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Psychiatric disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	7 (6.9)	21 (10.9)
Number of Subjects Censored, n (%)	95 (93.1)	172 (89.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.326 (0.441)
95% CI		(0.558, 3.151)
Log-rank p-value		0.580

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Psychiatric disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.8 (87.7, 98.0)	90.8 (86.7, 95.0)
6 months	92.8 (87.7, 98.0)	87.4 (82.2, 92.6)
9 months	NE (NE, NE)	87.4 (82.2, 92.6)
12 months	NE (NE, NE)	87.4 (82.2, 92.6)
18 months	NE (NE, NE)	87.4 (82.2, 92.6)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	6 (5.9)	12 (6.2)
Number of Subjects Censored, n (%)	96 (94.1)	181 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.867 (0.509)
95% CI		(0.320, 2.353)
Log-rank p-value		0.725

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.8 (89.0, 98.6)	95.1 (92.0, 98.2)
6 months	93.8 (89.0, 98.6)	92.4 (88.2, 96.7)
9 months	NE (NE, NE)	92.4 (88.2, 96.7)
12 months	NE (NE, NE)	92.4 (88.2, 96.7)
18 months	NE (NE, NE)	92.4 (88.2, 96.7)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	1 (1.0)	3 (1.6)
Number of Subjects Censored, n (%)	101 (99.0)	190 (98.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.514 (1.156)
95% CI		(0.157, 14.578)
Log-rank p-value		0.743

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.0, 100.0)	98.4 (96.7, 100.0)
6 months	99.0 (97.0, 100.0)	98.4 (96.7, 100.0)
9 months	NE (NE, NE)	98.4 (96.7, 100.0)
12 months	NE (NE, NE)	98.4 (96.7, 100.0)
18 months	NE (NE, NE)	98.4 (96.7, 100.0)
Median Follow-up Time (months)	2.83	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	0	3 (1.6)
Number of Subjects Censored, n (%)	102 (100.0)	190 (98.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.8*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.267

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.4 (96.5, 100.0)
6 months	100.0 (100.0, 100.0)	98.4 (96.5, 100.0)
9 months	NE (NE, NE)	98.4 (96.5, 100.0)
12 months	NE (NE, NE)	98.4 (96.5, 100.0)
18 months	NE (NE, NE)	98.4 (96.5, 100.0)
Median Follow-up Time (months)	2.83	4.93

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	7 (6.9)	20 (10.4)
Number of Subjects Censored, n (%)	95 (93.1)	173 (89.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.66, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.041 (0.457)
95% CI		(0.425, 2.551)
Log-rank p-value		1.000

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.0 (87.9, 98.0)	93.4 (89.8, 97.0)
6 months	93.0 (87.9, 98.0)	87.7 (81.9, 93.4)
9 months	NE (NE, NE)	85.6 (78.7, 92.5)
12 months	NE (NE, NE)	81.3 (70.8, 91.8)
18 months	NE (NE, NE)	81.3 (70.8, 91.8)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	1 (1.0)	8 (4.1)
Number of Subjects Censored, n (%)	101 (99.0)	185 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.66, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.8*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.876 (1.083)
95% CI		(0.344, 24.019)
Log-rank p-value		0.346

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.0, 100.0)	97.2 (94.7, 99.6)
6 months	99.0 (97.0, 100.0)	95.2 (91.5, 98.8)
9 months	NE (NE, NE)	95.2 (91.5, 98.8)
12 months	NE (NE, NE)	90.4 (80.7, 100.0)
18 months	NE (NE, NE)	90.4 (80.7, 100.0)
Median Follow-up Time (months)	2.83	4.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Number of Subjects with Events, n (%)	1 (1.0)	5 (2.6)
Number of Subjects Censored, n (%)	101 (99.0)	188 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.8*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.341 (1.144)
95% CI		(0.142, 12.614)
Log-rank p-value		0.863

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
ECOG: 0

Statistics	Placebo + BSC N=102	Fruquintinib + BSC N=193
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.1, 100.0)	98.9 (97.4, 100.0)
6 months	99.0 (97.1, 100.0)	96.9 (93.8, 100.0)
9 months	NE (NE, NE)	94.8 (89.7, 99.9)
12 months	NE (NE, NE)	94.8 (89.7, 99.9)
18 months	NE (NE, NE)	94.8 (89.7, 99.9)
Median Follow-up Time (months)	2.83	4.93

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	76 (59.4)	194 (73.8)
Number of Subjects Censored, n (%)	52 (40.6)	69 (26.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.39, 0.72)	0.43 (0.30, 0.66)
Median (95% CI)	1.38 (0.99, 1.94)	0.99 (0.72, 1.45)
75% percentile (95% CI)	NE (NE, NE)	4.37 (3.25, 6.93)
Min, Max	0.0, 13.0*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.226 (0.137)
95% CI		(0.937, 1.604)
Log-rank p-value		0.226

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	39.0 (30.2, 47.9)	32.4 (26.6, 38.2)
6 months	36.2 (26.5, 46.0)	19.3 (13.2, 25.4)
9 months	36.2 (26.5, 46.0)	13.0 (5.8, 20.2)
12 months	36.2 (26.5, 46.0)	13.0 (5.8, 20.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.30	0.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	35 (27.3)	99 (37.6)
Number of Subjects Censored, n (%)	93 (72.7)	164 (62.4)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.72, NE)	0.95 (0.69, 1.54)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.298 (0.198)
95% CI		(0.881, 1.913)
Log-rank p-value		0.201

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	70.4 (61.7, 79.2)	63.2 (57.2, 69.3)
6 months	66.5 (55.4, 77.6)	58.0 (51.1, 65.0)
9 months	66.5 (55.4, 77.6)	58.0 (51.1, 65.0)
12 months	66.5 (55.4, 77.6)	58.0 (51.1, 65.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	16 (12.5)	51 (19.4)
Number of Subjects Censored, n (%)	112 (87.5)	212 (80.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.32, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.389 (0.289)
95% CI		(0.789, 2.445)
Log-rank p-value		0.281

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.2 (79.9, 92.6)	80.7 (75.7, 85.6)
6 months	86.2 (79.9, 92.6)	78.4 (72.7, 84.2)
9 months	86.2 (79.9, 92.6)	76.1 (68.8, 83.3)
12 months	86.2 (79.9, 92.6)	76.1 (68.8, 83.3)
18 months	NE (NE, NE)	76.1 (68.8, 83.3)
Median Follow-up Time (months)	2.20	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	13 (10.2)	27 (10.3)
Number of Subjects Censored, n (%)	115 (89.8)	236 (89.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.901 (0.343)
95% CI		(0.460, 1.764)
Log-rank p-value		0.698

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.0 (83.2, 94.7)	90.7 (87.0, 94.4)
6 months	89.0 (83.2, 94.7)	88.3 (83.9, 92.8)
9 months	89.0 (83.2, 94.7)	86.8 (81.4, 92.1)
12 months	89.0 (83.2, 94.7)	86.8 (81.4, 92.1)
18 months	NE (NE, NE)	86.8 (81.4, 92.1)
Median Follow-up Time (months)	2.40	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	3 (2.3)	36 (13.7)
Number of Subjects Censored, n (%)	125 (97.7)	227 (86.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.614 (0.603)
95% CI		(1.721, 18.309)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (94.6, 100.0)	87.2 (83.1, 91.4)
6 months	97.5 (94.6, 100.0)	83.7 (78.4, 89.0)
9 months	97.5 (94.6, 100.0)	83.7 (78.4, 89.0)
12 months	97.5 (94.6, 100.0)	83.7 (78.4, 89.0)
18 months	NE (NE, NE)	83.7 (78.4, 89.0)
Median Follow-up Time (months)	2.46	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	21 (16.4)	20 (7.6)
Number of Subjects Censored, n (%)	107 (83.6)	243 (92.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.40, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.329 (0.320)
95% CI		(0.176, 0.616)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.9 (74.5, 89.3)	93.8 (90.7, 96.8)
6 months	77.8 (67.3, 88.3)	90.1 (85.5, 94.7)
9 months	77.8 (67.3, 88.3)	90.1 (85.5, 94.7)
12 months	77.8 (67.3, 88.3)	90.1 (85.5, 94.7)
18 months	NE (NE, NE)	77.2 (53.5, 100.0)
Median Follow-up Time (months)	2.58	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	13 (10.2)	16 (6.1)
Number of Subjects Censored, n (%)	115 (89.8)	247 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.491 (0.380)
95% CI		(0.233, 1.033)
Log-rank p-value		0.055

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.8 (82.9, 94.8)	93.8 (90.7, 96.9)
6 months	88.8 (82.9, 94.8)	93.8 (90.7, 96.9)
9 months	88.8 (82.9, 94.8)	90.0 (82.2, 97.8)
12 months	88.8 (82.9, 94.8)	90.0 (82.2, 97.8)
18 months	NE (NE, NE)	90.0 (82.2, 97.8)
Median Follow-up Time (months)	2.46	3.09

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	4 (3.1)	11 (4.2)
Number of Subjects Censored, n (%)	124 (96.9)	252 (95.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.72, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.908 (0.601)
95% CI		(0.280, 2.949)
Log-rank p-value		0.806

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.4 (92.9, 99.9)	96.8 (94.6, 99.0)
6 months	96.4 (92.9, 99.9)	95.1 (91.9, 98.3)
9 months	96.4 (92.9, 99.9)	95.1 (91.9, 98.3)
12 months	96.4 (92.9, 99.9)	89.5 (78.4, 100.0)
18 months	NE (NE, NE)	89.5 (78.4, 100.0)
Median Follow-up Time (months)	2.58	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	3 (2.3)	8 (3.0)
Number of Subjects Censored, n (%)	125 (97.7)	255 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.055 (0.687)
95% CI		(0.274, 4.056)
Log-rank p-value		0.975

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.3 (92.0, 100.0)	97.0 (94.8, 99.2)
6 months	96.3 (92.0, 100.0)	96.0 (93.0, 98.9)
9 months	96.3 (92.0, 100.0)	96.0 (93.0, 98.9)
12 months	96.3 (92.0, 100.0)	96.0 (93.0, 98.9)
18 months	NE (NE, NE)	96.0 (93.0, 98.9)
Median Follow-up Time (months)	2.58	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	1 (0.8)	5 (1.9)
Number of Subjects Censored, n (%)	127 (99.2)	258 (98.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.564 (1.130)
95% CI		(0.171, 14.318)
Log-rank p-value		0.694

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.7, 100.0)	98.9 (97.6, 100.0)
6 months	99.2 (97.7, 100.0)	96.4 (92.6, 100.0)
9 months	99.2 (97.7, 100.0)	96.4 (92.6, 100.0)
12 months	99.2 (97.7, 100.0)	96.4 (92.6, 100.0)
18 months	NE (NE, NE)	96.4 (92.6, 100.0)
Median Follow-up Time (months)	2.58	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	77 (60.2)	177 (67.3)
Number of Subjects Censored, n (%)	51 (39.8)	86 (32.7)
Time to first TEAE (months)		
25% percentile (95% CI)	0.46 (0.26, 0.69)	0.46 (0.30, 0.62)
Median (95% CI)	1.38 (0.89, 2.00)	1.12 (0.82, 1.64)
75% percentile (95% CI)	5.36 (3.75, NE)	6.47 (4.07, NE)
Min, Max	0.0, 5.6	0.0, 11.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.988 (0.140)
95% CI		(0.751, 1.299)
Log-rank p-value		0.955

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	36.1 (26.0, 46.2)	37.0 (31.0, 43.1)
6 months	0.0 (NE, NE)	25.7 (18.5, 32.8)
9 months	0.0 (NE, NE)	19.0 (10.6, 27.5)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.08	1.05

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	10 (7.8)	59 (22.4)
Number of Subjects Censored, n (%)	118 (92.2)	204 (77.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.95 (3.02, 10.87)
Median (95% CI)	NE (NE, NE)	NE (10.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.405 (0.345)
95% CI		(1.223, 4.730)
Log-rank p-value		0.010

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.9 (87.1, 96.7)	81.2 (76.4, 86.0)
6 months	91.9 (87.1, 96.7)	73.6 (66.4, 80.7)
9 months	91.9 (87.1, 96.7)	67.4 (57.9, 76.9)
12 months	91.9 (87.1, 96.7)	56.2 (34.6, 77.8)
18 months	NE (NE, NE)	56.2 (34.6, 77.8)
Median Follow-up Time (months)	2.33	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	23 (18.0)	50 (19.0)
Number of Subjects Censored, n (%)	105 (82.0)	213 (81.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.77, NE)	6.21 (3.48, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.848 (0.261)
95% CI		(0.509, 1.413)
Log-rank p-value		0.637

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.1 (74.0, 88.1)	82.3 (77.3, 87.3)
6 months	81.1 (74.0, 88.1)	75.7 (68.7, 82.8)
9 months	81.1 (74.0, 88.1)	71.2 (62.1, 80.3)
12 months	81.1 (74.0, 88.1)	71.2 (62.1, 80.3)
18 months	NE (NE, NE)	71.2 (62.1, 80.3)
Median Follow-up Time (months)	2.05	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	22 (17.2)	42 (16.0)
Number of Subjects Censored, n (%)	106 (82.8)	221 (84.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.53, NE)	10.12 (5.52, NE)
Median (95% CI)	NE (NE, NE)	NE (12.25, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.678 (0.275)
95% CI		(0.395, 1.163)
Log-rank p-value		0.188

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.0 (70.0, 88.0)	85.6 (81.1, 90.2)
6 months	79.0 (70.0, 88.0)	80.6 (74.4, 86.8)
9 months	79.0 (70.0, 88.0)	77.9 (70.0, 85.8)
12 months	79.0 (70.0, 88.0)	71.9 (58.5, 85.3)
18 months	NE (NE, NE)	57.5 (30.1, 84.9)
Median Follow-up Time (months)	2.33	2.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	14 (10.9)	40 (15.2)
Number of Subjects Censored, n (%)	114 (89.1)	223 (84.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.92, NE)	NE (6.80, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.027 (0.317)
95% CI		(0.552, 1.913)
Log-rank p-value		0.973

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.4 (77.7, 95.1)	86.9 (82.7, 91.2)
6 months	82.6 (71.6, 93.6)	81.7 (76.0, 87.4)
9 months	82.6 (71.6, 93.6)	79.6 (72.7, 86.5)
12 months	82.6 (71.6, 93.6)	75.6 (65.6, 85.7)
18 months	NE (NE, NE)	75.6 (65.6, 85.7)
Median Follow-up Time (months)	2.25	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	19 (14.8)	37 (14.1)
Number of Subjects Censored, n (%)	109 (85.2)	226 (85.9)
Time to first TEAE (months)		
25% percentile (95% CI)	5.36 (3.52, NE)	NE (6.21, NE)
Median (95% CI)	NE (5.36, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.755 (0.287)
95% CI		(0.430, 1.326)
Log-rank p-value		0.428

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.1 (78.4, 91.7)	87.4 (83.2, 91.6)
6 months	71.1 (50.6, 91.5)	82.3 (76.2, 88.3)
9 months	71.1 (50.6, 91.5)	80.6 (73.9, 87.3)
12 months	71.1 (50.6, 91.5)	80.6 (73.9, 87.3)
18 months	NE (NE, NE)	80.6 (73.9, 87.3)
Median Follow-up Time (months)	2.33	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	5 (3.9)	38 (14.4)
Number of Subjects Censored, n (%)	123 (96.1)	225 (85.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.98, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.488 (0.527)
95% CI		(1.597, 12.610)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (92.0, 99.4)	86.3 (82.0, 90.5)
6 months	95.7 (92.0, 99.4)	84.8 (80.2, 89.4)
9 months	95.7 (92.0, 99.4)	82.1 (75.2, 89.0)
12 months	95.7 (92.0, 99.4)	82.1 (75.2, 89.0)
18 months	NE (NE, NE)	82.1 (75.2, 89.0)
Median Follow-up Time (months)	2.46	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	6 (4.7)	16 (6.1)
Number of Subjects Censored, n (%)	122 (95.3)	247 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.997 (0.491)
95% CI		(0.381, 2.608)
Log-rank p-value		0.941

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.8 (92.1, 99.4)	94.3 (91.4, 97.2)
6 months	82.1 (57.1, 100.0)	92.8 (88.7, 96.9)
9 months	NE (NE, NE)	89.5 (82.0, 97.0)
12 months	NE (NE, NE)	89.5 (82.0, 97.0)
18 months	NE (NE, NE)	89.5 (82.0, 97.0)
Median Follow-up Time (months)	2.46	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	3 (2.3)	11 (4.2)
Number of Subjects Censored, n (%)	125 (97.7)	252 (95.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.156 (0.694)
95% CI		(0.553, 8.401)
Log-rank p-value		0.378

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (94.4, 100.0)	95.8 (93.3, 98.2)
6 months	97.3 (94.4, 100.0)	95.8 (93.3, 98.2)
9 months	97.3 (94.4, 100.0)	95.8 (93.3, 98.2)
12 months	97.3 (94.4, 100.0)	95.8 (93.3, 98.2)
18 months	NE (NE, NE)	95.8 (93.3, 98.2)
Median Follow-up Time (months)	2.46	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	4 (3.1)	9 (3.4)
Number of Subjects Censored, n (%)	124 (96.9)	254 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.020 (0.606)
95% CI		(0.311, 3.345)
Log-rank p-value		0.984

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.2 (92.4, 99.9)	96.3 (93.8, 98.7)
6 months	96.2 (92.4, 99.9)	96.3 (93.8, 98.7)
9 months	96.2 (92.4, 99.9)	96.3 (93.8, 98.7)
12 months	96.2 (92.4, 99.9)	96.3 (93.8, 98.7)
18 months	NE (NE, NE)	96.3 (93.8, 98.7)
Median Follow-up Time (months)	2.46	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	6 (4.7)	2 (0.8)
Number of Subjects Censored, n (%)	122 (95.3)	261 (99.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.134 (0.820)
95% CI		(0.027, 0.665)
Log-rank p-value		0.006

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.8 (90.7, 98.9)	99.2 (98.0, 100.0)
6 months	94.8 (90.7, 98.9)	99.2 (98.0, 100.0)
9 months	94.8 (90.7, 98.9)	99.2 (98.0, 100.0)
12 months	94.8 (90.7, 98.9)	99.2 (98.0, 100.0)
18 months	NE (NE, NE)	99.2 (98.0, 100.0)
Median Follow-up Time (months)	2.58	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	0	13 (4.9)
Number of Subjects Censored, n (%)	128 (100.0)	250 (95.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.008

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.0 (92.1, 97.8)
6 months	100.0 (100.0, 100.0)	95.0 (92.1, 97.8)
9 months	100.0 (100.0, 100.0)	92.0 (85.6, 98.3)
12 months	100.0 (100.0, 100.0)	92.0 (85.6, 98.3)
18 months	NE (NE, NE)	92.0 (85.6, 98.3)
Median Follow-up Time (months)	2.58	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	46 (35.9)	116 (44.1)
Number of Subjects Censored, n (%)	82 (64.1)	147 (55.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.89 (0.69, 1.87)	1.08 (0.72, 1.58)
Median (95% CI)	10.18 (3.22, NE)	6.05 (2.99, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.0, 10.2	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.069 (0.177)
95% CI		(0.755, 1.513)
Log-rank p-value		0.759

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	63.2 (54.3, 72.1)	55.7 (49.3, 62.2)
6 months	59.9 (49.3, 70.5)	50.4 (43.2, 57.6)
9 months	59.9 (49.3, 70.5)	47.1 (39.0, 55.1)
12 months	0.0 (NE, NE)	47.1 (39.0, 55.1)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.87	2.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	29 (22.7)	78 (29.7)
Number of Subjects Censored, n (%)	99 (77.3)	185 (70.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	2.53 (1.48, 3.09)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.190 (0.222)
95% CI		(0.770, 1.837)
Log-rank p-value		0.499

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.9 (68.2, 83.7)	69.6 (63.6, 75.6)
6 months	75.9 (68.2, 83.7)	65.1 (58.3, 72.0)
9 months	75.9 (68.2, 83.7)	65.1 (58.3, 72.0)
12 months	75.9 (68.2, 83.7)	65.1 (58.3, 72.0)
18 months	NE (NE, NE)	65.1 (58.3, 72.0)
Median Follow-up Time (months)	1.91	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	4 (3.1)	19 (7.2)
Number of Subjects Censored, n (%)	124 (96.9)	244 (92.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.865 (0.556)
95% CI		(0.627, 5.545)
Log-rank p-value		0.236

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.8 (93.8, 99.9)	92.7 (89.3, 96.1)
6 months	96.8 (93.8, 99.9)	90.9 (86.7, 95.0)
9 months	96.8 (93.8, 99.9)	90.9 (86.7, 95.0)
12 months	96.8 (93.8, 99.9)	90.9 (86.7, 95.0)
18 months	NE (NE, NE)	90.9 (86.7, 95.0)
Median Follow-up Time (months)	2.56	3.09

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	3 (2.3)	18 (6.8)
Number of Subjects Censored, n (%)	125 (97.7)	245 (93.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.211 (0.632)
95% CI		(0.641, 7.623)
Log-rank p-value		0.161

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.2, 100.0)	93.8 (90.7, 96.8)
6 months	94.7 (87.4, 100.0)	91.7 (87.6, 95.8)
9 months	94.7 (87.4, 100.0)	89.2 (82.9, 95.5)
12 months	94.7 (87.4, 100.0)	89.2 (82.9, 95.5)
18 months	NE (NE, NE)	89.2 (82.9, 95.5)
Median Follow-up Time (months)	2.56	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	3 (2.3)	9 (3.4)
Number of Subjects Censored, n (%)	125 (97.7)	254 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.121 (0.681)
95% CI		(0.295, 4.261)
Log-rank p-value		0.833

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (93.8, 100.0)	96.6 (94.2, 98.9)
6 months	97.1 (93.8, 100.0)	96.6 (94.2, 98.9)
9 months	97.1 (93.8, 100.0)	92.8 (85.3, 100.0)
12 months	97.1 (93.8, 100.0)	92.8 (85.3, 100.0)
18 months	NE (NE, NE)	92.8 (85.3, 100.0)
Median Follow-up Time (months)	2.56	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	3 (2.3)	12 (4.6)
Number of Subjects Censored, n (%)	125 (97.7)	251 (95.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.744 (0.654)
95% CI		(0.484, 6.286)
Log-rank p-value		0.375

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (94.9, 100.0)	95.5 (92.8, 98.1)
6 months	97.6 (94.9, 100.0)	95.5 (92.8, 98.1)
9 months	97.6 (94.9, 100.0)	92.8 (87.1, 98.5)
12 months	97.6 (94.9, 100.0)	92.8 (87.1, 98.5)
18 months	NE (NE, NE)	92.8 (87.1, 98.5)
Median Follow-up Time (months)	2.56	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	0	10 (3.8)
Number of Subjects Censored, n (%)	128 (100.0)	253 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.044

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.2 (93.8, 98.7)
6 months	100.0 (100.0, 100.0)	95.4 (92.5, 98.3)
9 months	100.0 (100.0, 100.0)	95.4 (92.5, 98.3)
12 months	100.0 (100.0, 100.0)	95.4 (92.5, 98.3)
18 months	NE (NE, NE)	95.4 (92.5, 98.3)
Median Follow-up Time (months)	2.58	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	2 (1.6)	9 (3.4)
Number of Subjects Censored, n (%)	126 (98.4)	254 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.546 (0.794)
95% CI		(0.326, 7.326)
Log-rank p-value		0.588

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (93.4, 100.0)	96.7 (94.5, 99.0)
6 months	97.3 (93.4, 100.0)	96.7 (94.5, 99.0)
9 months	97.3 (93.4, 100.0)	95.1 (91.2, 99.0)
12 months	97.3 (93.4, 100.0)	95.1 (91.2, 99.0)
18 months	NE (NE, NE)	95.1 (91.2, 99.0)
Median Follow-up Time (months)	2.58	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	1 (0.8)	4 (1.5)
Number of Subjects Censored, n (%)	127 (99.2)	259 (98.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.680 (1.242)
95% CI		(0.060, 7.763)
Log-rank p-value		0.833

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.7, 100.0)	99.6 (98.8, 100.0)
6 months	99.2 (97.7, 100.0)	98.1 (95.2, 100.0)
9 months	99.2 (97.7, 100.0)	93.0 (85.2, 100.0)
12 months	99.2 (97.7, 100.0)	93.0 (85.2, 100.0)
18 months	NE (NE, NE)	93.0 (85.2, 100.0)
Median Follow-up Time (months)	2.56	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	1 (0.8)	5 (1.9)
Number of Subjects Censored, n (%)	127 (99.2)	258 (98.1)
Time to first TEAE (months)		
25% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Median (95% CI)	10.18 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 10.2	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.577 (1.111)
95% CI		(0.179, 13.921)
Log-rank p-value		0.627

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.7 (95.8, 99.7)
6 months	100.0 (100.0, 100.0)	97.7 (95.8, 99.7)
9 months	100.0 (100.0, 100.0)	97.7 (95.8, 99.7)
12 months	0.0 (NE, NE)	97.7 (95.8, 99.7)
18 months	0.0 (NE, NE)	97.7 (95.8, 99.7)
Median Follow-up Time (months)	2.58	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	0	6 (2.3)
Number of Subjects Censored, n (%)	128 (100.0)	257 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.241

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.4 (96.6, 100.0)
6 months	100.0 (100.0, 100.0)	95.2 (91.1, 99.2)
9 months	100.0 (100.0, 100.0)	95.2 (91.1, 99.2)
12 months	100.0 (100.0, 100.0)	95.2 (91.1, 99.2)
18 months	NE (NE, NE)	95.2 (91.1, 99.2)
Median Follow-up Time (months)	2.58	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	43 (33.6)	107 (40.7)
Number of Subjects Censored, n (%)	85 (66.4)	156 (59.3)
Time to first TEAE (months)		
25% percentile (95% CI)	1.35 (0.92, 2.73)	1.15 (0.95, 1.61)
Median (95% CI)	NE (3.55, NE)	7.85 (5.55, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (16.79, NE)
Min, Max	0.2*, 6.8*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.035 (0.183)
95% CI		(0.723, 1.481)
Log-rank p-value		0.913

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	64.5 (55.4, 73.6)	60.5 (54.3, 66.7)
6 months	52.0 (33.6, 70.4)	56.8 (50.0, 63.6)
9 months	NE (NE, NE)	50.0 (41.1, 58.9)
12 months	NE (NE, NE)	50.0 (41.1, 58.9)
18 months	NE (NE, NE)	33.3 (6.0, 60.6)
Median Follow-up Time (months)	1.91	2.46

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	15 (11.7)	36 (13.7)
Number of Subjects Censored, n (%)	113 (88.3)	227 (86.3)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (5.59, NE)	NE (7.85, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.941 (0.313)
95% CI		(0.509, 1.738)
Log-rank p-value		0.793

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.3 (77.8, 92.7)	87.0 (82.8, 91.2)
6 months	73.1 (50.1, 96.1)	84.0 (78.7, 89.4)
9 months	NE (NE, NE)	81.3 (73.9, 88.7)
12 months	NE (NE, NE)	81.3 (73.9, 88.7)
18 months	NE (NE, NE)	81.3 (73.9, 88.7)
Median Follow-up Time (months)	2.33	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	9 (7.0)	31 (11.8)
Number of Subjects Censored, n (%)	119 (93.0)	232 (88.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.380 (0.385)
95% CI		(0.650, 2.934)
Log-rank p-value		0.419

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.4 (89.0, 97.8)	88.4 (84.3, 92.5)
6 months	80.1 (55.6, 100.0)	86.7 (82.0, 91.4)
9 months	NE (NE, NE)	84.3 (77.7, 90.8)
12 months	NE (NE, NE)	84.3 (77.7, 90.8)
18 months	NE (NE, NE)	84.3 (77.7, 90.8)
Median Follow-up Time (months)	2.51	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	7 (5.5)	30 (11.4)
Number of Subjects Censored, n (%)	121 (94.5)	233 (88.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.682 (0.426)
95% CI		(0.730, 3.876)
Log-rank p-value		0.219

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.2 (91.4, 98.9)	88.7 (84.6, 92.8)
6 months	81.6 (56.7, 100.0)	87.0 (82.3, 91.6)
9 months	NE (NE, NE)	84.5 (77.9, 91.1)
12 months	NE (NE, NE)	84.5 (77.9, 91.1)
18 months	NE (NE, NE)	84.5 (77.9, 91.1)
Median Follow-up Time (months)	2.56	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	8 (6.3)	19 (7.2)
Number of Subjects Censored, n (%)	120 (93.8)	244 (92.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.925 (0.425)
95% CI		(0.402, 2.128)
Log-rank p-value		0.840

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.6 (89.3, 97.9)	92.8 (89.5, 96.1)
6 months	93.6 (89.3, 97.9)	91.2 (87.3, 95.1)
9 months	93.6 (89.3, 97.9)	91.2 (87.3, 95.1)
12 months	93.6 (89.3, 97.9)	91.2 (87.3, 95.1)
18 months	NE (NE, NE)	91.2 (87.3, 95.1)
Median Follow-up Time (months)	2.56	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	1 (0.8)	19 (7.2)
Number of Subjects Censored, n (%)	127 (99.2)	244 (92.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		7.513 (1.029)
95% CI		(0.999, 56.488)
Log-rank p-value		0.027

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.2, 100.0)	92.9 (89.7, 96.2)
6 months	98.7 (96.2, 100.0)	91.3 (86.9, 95.8)
9 months	98.7 (96.2, 100.0)	89.7 (84.4, 95.1)
12 months	98.7 (96.2, 100.0)	89.7 (84.4, 95.1)
18 months	NE (NE, NE)	89.7 (84.4, 95.1)
Median Follow-up Time (months)	2.56	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	7 (5.5)	15 (5.7)
Number of Subjects Censored, n (%)	121 (94.5)	248 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.851 (0.465)
95% CI		(0.342, 2.119)
Log-rank p-value		0.749

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.0 (89.5, 98.4)	94.8 (92.0, 97.6)
6 months	94.0 (89.5, 98.4)	92.6 (88.5, 96.7)
9 months	94.0 (89.5, 98.4)	92.6 (88.5, 96.7)
12 months	94.0 (89.5, 98.4)	92.6 (88.5, 96.7)
18 months	NE (NE, NE)	92.6 (88.5, 96.7)
Median Follow-up Time (months)	2.51	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	1 (0.8)	15 (5.7)
Number of Subjects Censored, n (%)	127 (99.2)	248 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	7.43 (NE, NE)	NE (NE, NE)
Median (95% CI)	7.43 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	7.43 (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 7.4	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.464 (1.038)
95% CI		(0.845, 49.443)
Log-rank p-value		0.034

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.9 (92.2, 97.6)
6 months	100.0 (100.0, 100.0)	92.8 (88.9, 96.8)
9 months	0.0 (NE, NE)	92.8 (88.9, 96.8)
12 months	0.0 (NE, NE)	92.8 (88.9, 96.8)
18 months	0.0 (NE, NE)	92.8 (88.9, 96.8)
Median Follow-up Time (months)	2.58	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	4 (3.1)	14 (5.3)
Number of Subjects Censored, n (%)	124 (96.9)	249 (94.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.316 (0.574)
95% CI		(0.427, 4.053)
Log-rank p-value		0.627

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.7 (92.9, 100.0)	95.0 (92.2, 97.8)
6 months	92.3 (83.1, 100.0)	92.8 (88.6, 96.9)
9 months	92.3 (83.1, 100.0)	92.8 (88.6, 96.9)
12 months	92.3 (83.1, 100.0)	92.8 (88.6, 96.9)
18 months	NE (NE, NE)	92.8 (88.6, 96.9)
Median Follow-up Time (months)	2.51	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	0	8 (3.0)
Number of Subjects Censored, n (%)	128 (100.0)	255 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.104

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.6 (94.1, 99.1)
6 months	100.0 (100.0, 100.0)	95.5 (92.3, 98.8)
9 months	100.0 (100.0, 100.0)	95.5 (92.3, 98.8)
12 months	100.0 (100.0, 100.0)	95.5 (92.3, 98.8)
18 months	NE (NE, NE)	95.5 (92.3, 98.8)
Median Follow-up Time (months)	2.58	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	1 (0.8)	6 (2.3)
Number of Subjects Censored, n (%)	127 (99.2)	257 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.552 (1.081)
95% CI		(0.306, 21.247)
Log-rank p-value		0.347

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.6, 100.0)	97.4 (95.3, 99.5)
6 months	99.2 (97.6, 100.0)	97.4 (95.3, 99.5)
9 months	99.2 (97.6, 100.0)	97.4 (95.3, 99.5)
12 months	99.2 (97.6, 100.0)	97.4 (95.3, 99.5)
18 months	NE (NE, NE)	97.4 (95.3, 99.5)
Median Follow-up Time (months)	2.58	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	28 (21.9)	97 (36.9)
Number of Subjects Censored, n (%)	100 (78.1)	166 (63.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.25, NE)	1.12 (0.69, 1.77)
Median (95% CI)	NE (NE, NE)	9.69 (5.52, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.636 (0.217)
95% CI		(1.070, 2.501)
Log-rank p-value		0.032

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.3 (68.5, 84.2)	66.2 (60.3, 72.1)
6 months	76.3 (68.5, 84.2)	56.9 (49.2, 64.6)
9 months	76.3 (68.5, 84.2)	56.9 (49.2, 64.6)
12 months	76.3 (68.5, 84.2)	48.5 (35.7, 61.3)
18 months	NE (NE, NE)	48.5 (35.7, 61.3)
Median Follow-up Time (months)	1.91	2.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	3 (2.3)	32 (12.2)
Number of Subjects Censored, n (%)	125 (97.7)	231 (87.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.251 (0.605)
95% CI		(1.606, 17.170)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (95.0, 100.0)	88.0 (84.1, 92.0)
6 months	97.6 (95.0, 100.0)	87.3 (83.1, 91.5)
9 months	97.6 (95.0, 100.0)	87.3 (83.1, 91.5)
12 months	97.6 (95.0, 100.0)	87.3 (83.1, 91.5)
18 months	NE (NE, NE)	87.3 (83.1, 91.5)
Median Follow-up Time (months)	2.56	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	14 (10.9)	24 (9.1)
Number of Subjects Censored, n (%)	114 (89.1)	239 (90.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.677 (0.344)
95% CI		(0.345, 1.330)
Log-rank p-value		0.211

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.0 (82.1, 94.0)	92.2 (88.8, 95.6)
6 months	88.0 (82.1, 94.0)	87.0 (81.4, 92.6)
9 months	88.0 (82.1, 94.0)	87.0 (81.4, 92.6)
12 months	88.0 (82.1, 94.0)	87.0 (81.4, 92.6)
18 months	NE (NE, NE)	87.0 (81.4, 92.6)
Median Follow-up Time (months)	2.33	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	7 (5.5)	19 (7.2)
Number of Subjects Censored, n (%)	121 (94.5)	244 (92.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.158 (0.448)
95% CI		(0.481, 2.783)
Log-rank p-value		0.841

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.0 (89.6, 98.3)	93.0 (89.8, 96.3)
6 months	94.0 (89.6, 98.3)	91.1 (87.0, 95.3)
9 months	94.0 (89.6, 98.3)	91.1 (87.0, 95.3)
12 months	94.0 (89.6, 98.3)	91.1 (87.0, 95.3)
18 months	NE (NE, NE)	91.1 (87.0, 95.3)
Median Follow-up Time (months)	2.43	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	2 (1.6)	10 (3.8)
Number of Subjects Censored, n (%)	126 (98.4)	253 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.370 (0.776)
95% CI		(0.518, 10.841)
Log-rank p-value		0.270

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.2, 100.0)	96.0 (93.5, 98.4)
6 months	98.4 (96.2, 100.0)	96.0 (93.5, 98.4)
9 months	98.4 (96.2, 100.0)	96.0 (93.5, 98.4)
12 months	98.4 (96.2, 100.0)	96.0 (93.5, 98.4)
18 months	NE (NE, NE)	96.0 (93.5, 98.4)
Median Follow-up Time (months)	2.51	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	2 (1.6)	6 (2.3)
Number of Subjects Censored, n (%)	126 (98.4)	257 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.044 (0.836)
95% CI		(0.203, 5.376)
Log-rank p-value		0.952

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (95.6, 100.0)	98.1 (96.4, 99.7)
6 months	98.1 (95.6, 100.0)	98.1 (96.4, 99.7)
9 months	98.1 (95.6, 100.0)	95.9 (91.5, 100.0)
12 months	98.1 (95.6, 100.0)	95.9 (91.5, 100.0)
18 months	NE (NE, NE)	95.9 (91.5, 100.0)
Median Follow-up Time (months)	2.56	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Vascular disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	23 (18.0)	89 (33.8)
Number of Subjects Censored, n (%)	105 (82.0)	174 (66.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.81, NE)	1.18 (0.85, 2.07)
Median (95% CI)	NE (NE, NE)	NE (6.93, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.853 (0.236)
95% CI		(1.167, 2.942)
Log-rank p-value		0.011

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Vascular disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.3 (74.2, 88.4)	67.7 (61.9, 73.5)
6 months	75.5 (62.7, 88.3)	61.9 (54.6, 69.2)
9 months	NE (NE, NE)	57.6 (48.7, 66.5)
12 months	NE (NE, NE)	57.6 (48.7, 66.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	11 (8.6)	81 (30.8)
Number of Subjects Censored, n (%)	117 (91.4)	182 (69.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.61 (0.95, 3.71)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.637 (0.323)
95% CI		(1.932, 6.844)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.7 (85.4, 96.0)	69.9 (64.2, 75.6)
6 months	90.7 (85.4, 96.0)	66.8 (60.4, 73.3)
9 months	NE (NE, NE)	62.4 (53.9, 70.9)
12 months	NE (NE, NE)	62.4 (53.9, 70.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.22	2.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	26 (20.3)	80 (30.4)
Number of Subjects Censored, n (%)	102 (79.7)	183 (69.6)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (0.99, NE)	1.64 (0.92, 3.09)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.498 (0.231)
95% CI		(0.953, 2.356)
Log-rank p-value		0.080

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.1 (70.0, 86.2)	70.0 (64.3, 75.7)
6 months	65.1 (40.8, 89.3)	66.5 (59.7, 73.2)
9 months	NE (NE, NE)	63.1 (54.1, 72.2)
12 months	NE (NE, NE)	63.1 (54.1, 72.2)
18 months	NE (NE, NE)	63.1 (54.1, 72.2)
Median Follow-up Time (months)	1.92	2.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	10 (7.8)	26 (9.9)
Number of Subjects Censored, n (%)	118 (92.2)	237 (90.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.190 (0.390)
95% CI		(0.554, 2.557)
Log-rank p-value		0.626

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.1 (87.4, 96.8)	91.2 (87.6, 94.7)
6 months	92.1 (87.4, 96.8)	87.5 (82.5, 92.4)
9 months	92.1 (87.4, 96.8)	87.5 (82.5, 92.4)
12 months	92.1 (87.4, 96.8)	87.5 (82.5, 92.4)
18 months	NE (NE, NE)	87.5 (82.5, 92.4)
Median Follow-up Time (months)	2.40	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	5 (3.9)	26 (9.9)
Number of Subjects Censored, n (%)	123 (96.1)	237 (90.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (7.98, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.067 (0.494)
95% CI		(0.785, 5.441)
Log-rank p-value		0.143

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.8 (93.8, 99.9)	91.2 (87.6, 94.7)
6 months	83.0 (57.8, 100.0)	87.7 (82.3, 93.0)
9 months	NE (NE, NE)	84.4 (76.3, 92.5)
12 months	NE (NE, NE)	84.4 (76.3, 92.5)
18 months	NE (NE, NE)	84.4 (76.3, 92.5)
Median Follow-up Time (months)	2.46	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	2 (1.6)	16 (6.1)
Number of Subjects Censored, n (%)	126 (98.4)	247 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.017 (0.753)
95% CI		(0.919, 17.558)
Log-rank p-value		0.048

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.2, 100.0)	94.0 (91.1, 97.0)
6 months	98.4 (96.2, 100.0)	92.6 (88.7, 96.6)
9 months	98.4 (96.2, 100.0)	92.6 (88.7, 96.6)
12 months	98.4 (96.2, 100.0)	92.6 (88.7, 96.6)
18 months	NE (NE, NE)	92.6 (88.7, 96.6)
Median Follow-up Time (months)	2.56	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	2 (1.6)	7 (2.7)
Number of Subjects Censored, n (%)	126 (98.4)	256 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.418 (0.806)
95% CI		(0.292, 6.884)
Log-rank p-value		0.691

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.2, 100.0)	97.2 (95.1, 99.2)
6 months	98.4 (96.2, 100.0)	97.2 (95.1, 99.2)
9 months	98.4 (96.2, 100.0)	97.2 (95.1, 99.2)
12 months	98.4 (96.2, 100.0)	97.2 (95.1, 99.2)
18 months	NE (NE, NE)	97.2 (95.1, 99.2)
Median Follow-up Time (months)	2.58	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	1 (0.8)	5 (1.9)
Number of Subjects Censored, n (%)	127 (99.2)	258 (98.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.993 (1.106)
95% CI		(0.228, 17.430)
Log-rank p-value		0.548

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.7, 100.0)	98.5 (97.0, 100.0)
6 months	99.2 (97.7, 100.0)	97.0 (93.8, 100.0)
9 months	99.2 (97.7, 100.0)	97.0 (93.8, 100.0)
12 months	99.2 (97.7, 100.0)	97.0 (93.8, 100.0)
18 months	NE (NE, NE)	97.0 (93.8, 100.0)
Median Follow-up Time (months)	2.56	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	0	4 (1.5)
Number of Subjects Censored, n (%)	128 (100.0)	259 (98.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.180

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.3 (96.7, 100.0)
6 months	100.0 (100.0, 100.0)	98.3 (96.7, 100.0)
9 months	100.0 (100.0, 100.0)	98.3 (96.7, 100.0)
12 months	100.0 (100.0, 100.0)	98.3 (96.7, 100.0)
18 months	NE (NE, NE)	98.3 (96.7, 100.0)
Median Follow-up Time (months)	2.58	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	14 (10.9)	72 (27.4)
Number of Subjects Censored, n (%)	114 (89.1)	191 (72.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	2.66 (1.58, 6.24)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.708 (0.305)
95% CI		(1.489, 4.927)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.7 (83.1, 94.3)	74.2 (68.7, 79.6)
6 months	88.7 (83.1, 94.3)	68.6 (61.6, 75.6)
9 months	88.7 (83.1, 94.3)	63.8 (54.6, 73.1)
12 months	88.7 (83.1, 94.3)	63.8 (54.6, 73.1)
18 months	NE (NE, NE)	63.8 (54.6, 73.1)
Median Follow-up Time (months)	2.40	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	2 (1.6)	35 (13.3)
Number of Subjects Censored, n (%)	126 (98.4)	228 (86.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.39, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		17.101 (1.019)
95% CI		(2.320, 126.038)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.2, 100.0)	88.1 (84.1, 92.1)
6 months	98.4 (96.2, 100.0)	83.8 (78.1, 89.5)
9 months	98.4 (96.2, 100.0)	81.0 (73.1, 88.8)
12 months	98.4 (96.2, 100.0)	81.0 (73.1, 88.8)
18 months	NE (NE, NE)	81.0 (73.1, 88.8)
Median Follow-up Time (months)	2.58	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	6 (4.7)	9 (3.4)
Number of Subjects Censored, n (%)	122 (95.3)	254 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.680 (0.527)
95% CI		(0.242, 1.912)
Log-rank p-value		0.480

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.2 (91.5, 99.0)	96.5 (94.3, 98.8)
6 months	95.2 (91.5, 99.0)	96.5 (94.3, 98.8)
9 months	95.2 (91.5, 99.0)	96.5 (94.3, 98.8)
12 months	95.2 (91.5, 99.0)	96.5 (94.3, 98.8)
18 months	NE (NE, NE)	96.5 (94.3, 98.8)
Median Follow-up Time (months)	2.51	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	0	7 (2.7)
Number of Subjects Censored, n (%)	128 (100.0)	256 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.098

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.5 (95.6, 99.5)
6 months	100.0 (100.0, 100.0)	96.7 (94.1, 99.2)
9 months	100.0 (100.0, 100.0)	96.7 (94.1, 99.2)
12 months	100.0 (100.0, 100.0)	96.7 (94.1, 99.2)
18 months	NE (NE, NE)	96.7 (94.1, 99.2)
Median Follow-up Time (months)	2.58	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Nervous system disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	19 (14.8)	71 (27.0)
Number of Subjects Censored, n (%)	109 (85.2)	192 (73.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	2.99 (1.61, 6.11)
Median (95% CI)	NE (NE, NE)	NE (11.10, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.603 (0.261)
95% CI		(0.961, 2.674)
Log-rank p-value		0.072

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Nervous system disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.6 (76.6, 90.5)	74.5 (69.0, 80.0)
6 months	83.6 (76.6, 90.5)	69.0 (62.0, 76.0)
9 months	83.6 (76.6, 90.5)	65.6 (57.5, 73.7)
12 months	83.6 (76.6, 90.5)	59.1 (44.9, 73.3)
18 months	NE (NE, NE)	59.1 (44.9, 73.3)
Median Follow-up Time (months)	2.25	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	3 (2.3)	23 (8.7)
Number of Subjects Censored, n (%)	125 (97.7)	240 (91.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.413 (0.616)
95% CI		(1.019, 11.426)
Log-rank p-value		0.037

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (94.2, 100.0)	91.8 (88.5, 95.2)
6 months	97.3 (94.2, 100.0)	91.8 (88.5, 95.2)
9 months	97.3 (94.2, 100.0)	88.4 (82.7, 94.1)
12 months	97.3 (94.2, 100.0)	88.4 (82.7, 94.1)
18 months	NE (NE, NE)	88.4 (82.7, 94.1)
Median Follow-up Time (months)	2.56	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	5 (3.9)	6 (2.3)
Number of Subjects Censored, n (%)	123 (96.1)	257 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.494 (0.609)
95% CI		(0.150, 1.631)
Log-rank p-value		0.227

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.0 (92.6, 99.4)	97.5 (95.5, 99.5)
6 months	96.0 (92.6, 99.4)	97.5 (95.5, 99.5)
9 months	96.0 (92.6, 99.4)	97.5 (95.5, 99.5)
12 months	96.0 (92.6, 99.4)	97.5 (95.5, 99.5)
18 months	NE (NE, NE)	97.5 (95.5, 99.5)
Median Follow-up Time (months)	2.56	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	1 (0.8)	9 (3.4)
Number of Subjects Censored, n (%)	127 (99.2)	254 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.570 (1.057)
95% CI		(0.576, 36.276)
Log-rank p-value		0.125

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.2, 100.0)	96.4 (94.1, 98.7)
6 months	99.1 (97.2, 100.0)	96.4 (94.1, 98.7)
9 months	99.1 (97.2, 100.0)	96.4 (94.1, 98.7)
12 months	99.1 (97.2, 100.0)	96.4 (94.1, 98.7)
18 months	NE (NE, NE)	96.4 (94.1, 98.7)
Median Follow-up Time (months)	2.56	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	19 (14.8)	68 (25.9)
Number of Subjects Censored, n (%)	109 (85.2)	195 (74.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.83, NE)	3.94 (1.97, 5.55)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.486 (0.263)
95% CI		(0.887, 2.488)
Log-rank p-value		0.136

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.6 (75.2, 90.1)	76.0 (70.6, 81.4)
6 months	82.6 (75.2, 90.1)	67.9 (60.3, 75.5)
9 months	82.6 (75.2, 90.1)	63.6 (54.4, 72.7)
12 months	82.6 (75.2, 90.1)	63.6 (54.4, 72.7)
18 months	NE (NE, NE)	63.6 (54.4, 72.7)
Median Follow-up Time (months)	2.20	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	7 (5.5)	41 (15.6)
Number of Subjects Censored, n (%)	121 (94.5)	222 (84.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.93, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.418 (0.413)
95% CI		(1.077, 5.429)
Log-rank p-value		0.029

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.0 (89.7, 98.4)	85.0 (80.4, 89.6)
6 months	94.0 (89.7, 98.4)	81.8 (76.0, 87.6)
9 months	94.0 (89.7, 98.4)	75.7 (65.8, 85.7)
12 months	94.0 (89.7, 98.4)	75.7 (65.8, 85.7)
18 months	NE (NE, NE)	75.7 (65.8, 85.7)
Median Follow-up Time (months)	2.40	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	5 (3.9)	6 (2.3)
Number of Subjects Censored, n (%)	123 (96.1)	257 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.497 (0.611)
95% CI		(0.150, 1.647)
Log-rank p-value		0.321

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.8 (92.1, 99.4)	97.7 (95.8, 99.5)
6 months	95.8 (92.1, 99.4)	97.7 (95.8, 99.5)
9 months	95.8 (92.1, 99.4)	97.7 (95.8, 99.5)
12 months	95.8 (92.1, 99.4)	97.7 (95.8, 99.5)
18 months	NE (NE, NE)	97.7 (95.8, 99.5)
Median Follow-up Time (months)	2.51	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Infections and infestations**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	16 (12.5)	48 (18.3)
Number of Subjects Censored, n (%)	112 (87.5)	215 (81.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.15, NE)	6.93 (5.09, NE)
Median (95% CI)	NE (NE, NE)	17.48 (17.48, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.48, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.178 (0.302)
95% CI		(0.651, 2.131)
Log-rank p-value		0.580

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Infections and infestations**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (81.5, 93.5)	83.9 (79.2, 88.7)
6 months	84.1 (75.5, 92.8)	76.7 (69.5, 83.9)
9 months	84.1 (75.5, 92.8)	68.6 (57.6, 79.5)
12 months	84.1 (75.5, 92.8)	68.6 (57.6, 79.5)
18 months	NE (NE, NE)	45.7 (8.4, 83.0)
Median Follow-up Time (months)	2.43	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	4 (3.1)	12 (4.6)
Number of Subjects Censored, n (%)	124 (96.9)	251 (95.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.084 (0.596)
95% CI		(0.337, 3.486)
Log-rank p-value		0.887

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (94.9, 100.0)	96.4 (94.1, 98.7)
6 months	94.0 (86.6, 100.0)	93.8 (89.5, 98.1)
9 months	94.0 (86.6, 100.0)	91.6 (85.6, 97.6)
12 months	94.0 (86.6, 100.0)	91.6 (85.6, 97.6)
18 months	NE (NE, NE)	91.6 (85.6, 97.6)
Median Follow-up Time (months)	2.51	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	3 (2.3)	6 (2.3)
Number of Subjects Censored, n (%)	125 (97.7)	257 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.600 (0.734)
95% CI		(0.142, 2.528)
Log-rank p-value		0.487

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (94.5, 100.0)	98.2 (96.4, 100.0)
6 months	97.4 (94.5, 100.0)	96.0 (92.4, 99.6)
9 months	97.4 (94.5, 100.0)	96.0 (92.4, 99.6)
12 months	97.4 (94.5, 100.0)	96.0 (92.4, 99.6)
18 months	NE (NE, NE)	96.0 (92.4, 99.6)
Median Follow-up Time (months)	2.58	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	1 (0.8)	8 (3.0)
Number of Subjects Censored, n (%)	127 (99.2)	255 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.491 (1.067)
95% CI		(0.431, 28.268)
Log-rank p-value		0.203

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.7, 100.0)	96.4 (94.0, 98.9)
6 months	99.2 (97.7, 100.0)	96.4 (94.0, 98.9)
9 months	99.2 (97.7, 100.0)	96.4 (94.0, 98.9)
12 months	99.2 (97.7, 100.0)	96.4 (94.0, 98.9)
18 months	NE (NE, NE)	96.4 (94.0, 98.9)
Median Follow-up Time (months)	2.58	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	28 (21.9)	36 (13.7)
Number of Subjects Censored, n (%)	100 (78.1)	227 (86.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.61, NE)	NE (6.77, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.519 (0.258)
95% CI		(0.313, 0.859)
Log-rank p-value		0.017

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.1 (66.8, 83.4)	87.0 (82.8, 91.2)
6 months	75.1 (66.8, 83.4)	85.4 (80.7, 90.1)
9 months	75.1 (66.8, 83.4)	81.6 (74.7, 88.5)
12 months	75.1 (66.8, 83.4)	81.6 (74.7, 88.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	20 (15.6)	19 (7.2)
Number of Subjects Censored, n (%)	108 (84.4)	244 (92.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.10, NE)	17.74 (17.74, NE)
Median (95% CI)	NE (NE, NE)	17.74 (17.74, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.74, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.334 (0.334)
95% CI		(0.174, 0.643)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.2 (73.4, 88.9)	93.6 (90.5, 96.8)
6 months	81.2 (73.4, 88.9)	92.1 (88.3, 95.8)
9 months	81.2 (73.4, 88.9)	90.4 (85.5, 95.3)
12 months	81.2 (73.4, 88.9)	90.4 (85.5, 95.3)
18 months	NE (NE, NE)	45.2 (0.0, 100.0)
Median Follow-up Time (months)	2.14	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	3 (2.3)	18 (6.8)
Number of Subjects Censored, n (%)	125 (97.7)	245 (93.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.743 (0.625)
95% CI		(0.806, 9.339)
Log-rank p-value		0.096

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (94.6, 100.0)	92.9 (89.7, 96.1)
6 months	97.4 (94.6, 100.0)	92.9 (89.7, 96.1)
9 months	97.4 (94.6, 100.0)	92.9 (89.7, 96.1)
12 months	97.4 (94.6, 100.0)	92.9 (89.7, 96.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Endocrine disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	1 (0.8)	57 (21.7)
Number of Subjects Censored, n (%)	127 (99.2)	206 (78.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.63 (2.76, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		25.037 (1.010)
95% CI		(3.456, 181.365)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Endocrine disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.6, 100.0)	79.3 (74.1, 84.5)
6 months	99.2 (97.6, 100.0)	70.5 (62.4, 78.5)
9 months	99.2 (97.6, 100.0)	68.5 (59.8, 77.2)
12 months	99.2 (97.6, 100.0)	68.5 (59.8, 77.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	1 (0.8)	52 (19.8)
Number of Subjects Censored, n (%)	127 (99.2)	211 (80.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.59 (3.42, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		22.619 (1.011)
95% CI		(3.115, 164.226)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.6, 100.0)	81.4 (76.4, 86.4)
6 months	99.2 (97.6, 100.0)	72.7 (64.8, 80.5)
9 months	99.2 (97.6, 100.0)	70.8 (62.3, 79.3)
12 months	99.2 (97.6, 100.0)	70.8 (62.3, 79.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Psychiatric disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	10 (7.8)	37 (14.1)
Number of Subjects Censored, n (%)	118 (92.2)	226 (85.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.29, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.297 (0.364)
95% CI		(0.635, 2.649)
Log-rank p-value		0.461

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Psychiatric disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.9 (86.8, 97.1)	87.5 (83.1, 91.8)
6 months	88.5 (80.3, 96.7)	80.4 (73.8, 87.0)
9 months	88.5 (80.3, 96.7)	78.7 (71.4, 85.9)
12 months	88.5 (80.3, 96.7)	78.7 (71.4, 85.9)
18 months	NE (NE, NE)	78.7 (71.4, 85.9)
Median Follow-up Time (months)	2.40	2.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	6 (4.7)	14 (5.3)
Number of Subjects Censored, n (%)	122 (95.3)	249 (94.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.656 (0.504)
95% CI		(0.244, 1.761)
Log-rank p-value		0.462

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.8 (90.6, 98.9)	94.7 (91.6, 97.8)
6 months	94.8 (90.6, 98.9)	93.2 (89.5, 96.9)
9 months	94.8 (90.6, 98.9)	91.4 (86.3, 96.4)
12 months	94.8 (90.6, 98.9)	91.4 (86.3, 96.4)
18 months	NE (NE, NE)	91.4 (86.3, 96.4)
Median Follow-up Time (months)	2.43	3.09

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	1 (0.8)	8 (3.0)
Number of Subjects Censored, n (%)	127 (99.2)	255 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.037 (1.089)
95% CI		(0.359, 25.670)
Log-rank p-value		0.381

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.6 (94.1, 99.2)
6 months	96.4 (89.6, 100.0)	95.3 (91.7, 98.9)
9 months	96.4 (89.6, 100.0)	95.3 (91.7, 98.9)
12 months	96.4 (89.6, 100.0)	95.3 (91.7, 98.9)
18 months	NE (NE, NE)	95.3 (91.7, 98.9)
Median Follow-up Time (months)	2.58	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	2 (1.6)	8 (3.0)
Number of Subjects Censored, n (%)	126 (98.4)	255 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.801 (0.803)
95% CI		(0.373, 8.697)
Log-rank p-value		0.441

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.9 (95.1, 100.0)	97.6 (95.8, 99.5)
6 months	97.9 (95.1, 100.0)	95.4 (91.8, 99.0)
9 months	97.9 (95.1, 100.0)	95.4 (91.8, 99.0)
12 months	97.9 (95.1, 100.0)	95.4 (91.8, 99.0)
18 months	NE (NE, NE)	95.4 (91.8, 99.0)
Median Follow-up Time (months)	2.56	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	17 (13.3)	30 (11.4)
Number of Subjects Censored, n (%)	111 (86.7)	233 (88.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.15, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.714 (0.305)
95% CI		(0.392, 1.298)
Log-rank p-value		0.311

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.8 (80.7, 92.9)	87.7 (83.5, 91.9)
6 months	83.5 (74.8, 92.1)	86.9 (82.4, 91.4)
9 months	83.5 (74.8, 92.1)	86.9 (82.4, 91.4)
12 months	83.5 (74.8, 92.1)	86.9 (82.4, 91.4)
18 months	NE (NE, NE)	86.9 (82.4, 91.4)
Median Follow-up Time (months)	2.46	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	2 (1.6)	11 (4.2)
Number of Subjects Censored, n (%)	126 (98.4)	252 (95.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.039 (0.770)
95% CI		(0.450, 9.230)
Log-rank p-value		0.382

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (95.2, 100.0)	95.1 (92.2, 97.9)
6 months	98.0 (95.2, 100.0)	95.1 (92.2, 97.9)
9 months	98.0 (95.2, 100.0)	95.1 (92.2, 97.9)
12 months	98.0 (95.2, 100.0)	95.1 (92.2, 97.9)
18 months	NE (NE, NE)	95.1 (92.2, 97.9)
Median Follow-up Time (months)	2.51	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3E
Summary of Time to Onset of TEAE by SOC/PT by ECOG PS
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
ECOG: 1

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Number of Subjects with Events, n (%)	1 (0.8)	9 (3.4)
Number of Subjects Censored, n (%)	127 (99.2)	254 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.185 (1.055)
95% CI		(0.529, 33.083)
Log-rank p-value		0.148

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
<= 18 months

Statistics	Placebo + BSC N=128	Fruquintinib + BSC N=263
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.7, 100.0)	96.4 (94.0, 98.7)
6 months	99.2 (97.7, 100.0)	96.4 (94.0, 98.7)
9 months	99.2 (97.7, 100.0)	96.4 (94.0, 98.7)
12 months	99.2 (97.7, 100.0)	96.4 (94.0, 98.7)
18 months	NE (NE, NE)	96.4 (94.0, 98.7)
Median Follow-up Time (months)	2.58	3.22

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	4 (30.8)	22 (59.5)
Number of Subjects Censored, n (%)	9 (69.2)	15 (40.5)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.72, NE)	0.69 (0.20, 0.69)
Median (95% CI)	3.71 (1.64, NE)	1.41 (0.69, NE)
75% percentile (95% CI)	NE (3.71, NE)	NE (1.91, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Min, Max	0.7, 3.7*	0.1, 8.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.413 (0.554)
95% CI		(0.814, 7.152)
Log-rank p-value		0.160

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.8 (48.2, 99.5)	40.5 (24.7, 56.4)
6 months	NE (NE, NE)	40.5 (24.7, 56.4)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	1.41

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	1 (7.7)	11 (29.7)
Number of Subjects Censored, n (%)	12 (92.3)	26 (70.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.87, NE)	1.61 (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (2.56, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.7, 8.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.104 (1.067)
95% CI		(0.383, 25.143)
Log-rank p-value		0.277

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (73.9, 100.0)	68.5 (52.8, 84.1)
6 months	NE (NE, NE)	68.5 (52.8, 84.1)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.56

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	2 (15.4)	4 (10.8)
Number of Subjects Censored, n (%)	11 (84.6)	33 (89.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.72, NE)	NE (1.91, NE)
Median (95% CI)	NE (1.64, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.792 (0.881)
95% CI		(0.141, 4.452)
Log-rank p-value		0.766

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.1 (61.5, 100.0)	88.9 (78.5, 99.2)
6 months	NE (NE, NE)	88.9 (78.5, 99.2)
9 months	NE (NE, NE)	88.9 (78.5, 99.2)
12 months	NE (NE, NE)	88.9 (78.5, 99.2)
18 months	NE (NE, NE)	88.9 (78.5, 99.2)
Median Follow-up Time (months)	1.91	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	3 (8.1)
Number of Subjects Censored, n (%)	13 (100.0)	34 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.273

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	91.9 (83.1, 100.0)
6 months	NE (NE, NE)	91.9 (83.1, 100.0)
9 months	NE (NE, NE)	91.9 (83.1, 100.0)
12 months	NE (NE, NE)	91.9 (83.1, 100.0)
18 months	NE (NE, NE)	91.9 (83.1, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	4 (10.8)
Number of Subjects Censored, n (%)	13 (100.0)	33 (89.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.61, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.1, 10.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.379

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	88.9 (78.7, 99.2)
6 months	NE (NE, NE)	88.9 (78.7, 99.2)
9 months	NE (NE, NE)	88.9 (78.7, 99.2)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	4 (10.8)
Number of Subjects Censored, n (%)	13 (100.0)	33 (89.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.57, NE)
Median (95% CI)	NE (NE, NE)	NE (4.57, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	1.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.234

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	91.8 (82.9, 100.0)
6 months	NE (NE, NE)	80.3 (57.9, 100.0)
9 months	NE (NE, NE)	80.3 (57.9, 100.0)
12 months	NE (NE, NE)	80.3 (57.9, 100.0)
18 months	NE (NE, NE)	80.3 (57.9, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	1 (2.7)
Number of Subjects Censored, n (%)	13 (100.0)	36 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	1.1*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.527

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.2 (91.9, 100.0)
6 months	NE (NE, NE)	97.2 (91.9, 100.0)
9 months	NE (NE, NE)	97.2 (91.9, 100.0)
12 months	NE (NE, NE)	97.2 (91.9, 100.0)
18 months	NE (NE, NE)	97.2 (91.9, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	1 (7.7)	0
Number of Subjects Censored, n (%)	12 (92.3)	37 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.94, NE)	NE (NE, NE)
Median (95% CI)	NE (1.94, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	1.1*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.157

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.7 (59.8, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	1.94	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	9 (69.2)	17 (45.9)
Number of Subjects Censored, n (%)	4 (30.8)	20 (54.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.30 (0.03, 0.69)	0.69 (0.26, 1.45)
Median (95% CI)	0.69 (0.26, NE)	3.68 (0.72, NE)
75% percentile (95% CI)	NE (0.43, NE)	NE (NE, NE)
Min, Max	0.0, 3.7*	0.2, 5.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.452 (0.444)
95% CI		(0.189, 1.079)
Log-rank p-value		0.220

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	25.6 (0.0, 52.7)	56.1 (39.9, 72.3)
6 months	NE (NE, NE)	NE (NE, NE)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.69	1.91

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	3 (8.1)
Number of Subjects Censored, n (%)	13 (100.0)	34 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.48, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.540

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.6 (87.3, 100.0)
6 months	NE (NE, NE)	88.3 (74.5, 100.0)
9 months	NE (NE, NE)	88.3 (74.5, 100.0)
12 months	NE (NE, NE)	88.3 (74.5, 100.0)
18 months	NE (NE, NE)	88.3 (74.5, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	2 (15.4)	3 (8.1)
Number of Subjects Censored, n (%)	11 (84.6)	34 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.30, NE)	NE (3.48, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 3.7*	0.9, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.298 (1.021)
95% CI		(0.040, 2.207)
Log-rank p-value		0.274

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.6 (65.0, 100.0)	94.5 (87.1, 100.0)
6 months	NE (NE, NE)	88.2 (74.4, 100.0)
9 months	NE (NE, NE)	88.2 (74.4, 100.0)
12 months	NE (NE, NE)	88.2 (74.4, 100.0)
18 months	NE (NE, NE)	88.2 (74.4, 100.0)
Median Follow-up Time (months)	1.91	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	5 (38.5)	6 (16.2)
Number of Subjects Censored, n (%)	8 (61.5)	31 (83.8)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.03, NE)	12.25 (1.94, NE)
Median (95% CI)	4.57 (0.95, NE)	12.25 (NE, NE)
75% percentile (95% CI)	4.57 (NE, NE)	12.25 (NE, NE)
Min, Max	0.0, 4.6	0.2, 12.3
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.311 (0.651)
95% CI		(0.087, 1.112)
Log-rank p-value		0.142

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	67.3 (40.6, 94.0)	88.5 (77.9, 99.2)
6 months	0.0 (NE, NE)	81.7 (65.6, 97.9)
9 months	0.0 (NE, NE)	81.7 (65.6, 97.9)
12 months	0.0 (NE, NE)	81.7 (65.6, 97.9)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	1.87	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	2 (5.4)
Number of Subjects Censored, n (%)	13 (100.0)	35 (94.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	1.1*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.421

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.1 (83.9, 100.0)
6 months	NE (NE, NE)	93.1 (83.9, 100.0)
9 months	NE (NE, NE)	93.1 (83.9, 100.0)
12 months	NE (NE, NE)	93.1 (83.9, 100.0)
18 months	NE (NE, NE)	93.1 (83.9, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	2 (15.4)	3 (8.1)
Number of Subjects Censored, n (%)	11 (84.6)	34 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.16, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.307 (1.033)
95% CI		(0.041, 2.327)
Log-rank p-value		0.341

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.6 (65.0, 100.0)	91.8 (82.9, 100.0)
6 months	NE (NE, NE)	91.8 (82.9, 100.0)
9 months	NE (NE, NE)	91.8 (82.9, 100.0)
12 months	NE (NE, NE)	91.8 (82.9, 100.0)
18 months	NE (NE, NE)	91.8 (82.9, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	5 (13.5)
Number of Subjects Censored, n (%)	13 (100.0)	32 (86.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.66, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.169

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	86.5 (75.5, 97.5)
6 months	NE (NE, NE)	86.5 (75.5, 97.5)
9 months	NE (NE, NE)	86.5 (75.5, 97.5)
12 months	NE (NE, NE)	86.5 (75.5, 97.5)
18 months	NE (NE, NE)	86.5 (75.5, 97.5)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	3 (8.1)
Number of Subjects Censored, n (%)	13 (100.0)	34 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.91, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	1.1*, 10.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.358

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	91.0 (81.3, 100.0)
6 months	NE (NE, NE)	91.0 (81.3, 100.0)
9 months	NE (NE, NE)	91.0 (81.3, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	1 (2.7)
Number of Subjects Censored, n (%)	13 (100.0)	36 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.527

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.3 (92.1, 100.0)
6 months	NE (NE, NE)	97.3 (92.1, 100.0)
9 months	NE (NE, NE)	97.3 (92.1, 100.0)
12 months	NE (NE, NE)	97.3 (92.1, 100.0)
18 months	NE (NE, NE)	97.3 (92.1, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	1 (2.7)
Number of Subjects Censored, n (%)	13 (100.0)	36 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.540

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.3 (92.1, 100.0)
6 months	NE (NE, NE)	97.3 (92.1, 100.0)
9 months	NE (NE, NE)	97.3 (92.1, 100.0)
12 months	NE (NE, NE)	97.3 (92.1, 100.0)
18 months	NE (NE, NE)	97.3 (92.1, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	1 (7.7)	0
Number of Subjects Censored, n (%)	12 (92.3)	37 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.30, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 5.6*	1.1*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.046

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	1.91	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	2 (15.4)	12 (32.4)
Number of Subjects Censored, n (%)	11 (84.6)	25 (67.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.46, NE)	1.87 (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (3.68, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 5.6*	0.5, 8.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.748 (0.781)
95% CI		(0.378, 8.080)
Log-rank p-value		0.468

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.6 (65.0, 100.0)	69.3 (54.0, 84.5)
6 months	NE (NE, NE)	63.0 (44.8, 81.1)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	1 (7.7)	3 (8.1)
Number of Subjects Censored, n (%)	12 (92.3)	34 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.46, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.703 (1.233)
95% CI		(0.063, 7.875)
Log-rank p-value		0.843

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	91.9 (83.1, 100.0)
6 months	NE (NE, NE)	91.9 (83.1, 100.0)
9 months	NE (NE, NE)	91.9 (83.1, 100.0)
12 months	NE (NE, NE)	91.9 (83.1, 100.0)
18 months	NE (NE, NE)	91.9 (83.1, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	1 (2.7)
Number of Subjects Censored, n (%)	13 (100.0)	36 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	1.1*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.546

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.7 (90.2, 100.0)
6 months	NE (NE, NE)	96.7 (90.2, 100.0)
9 months	NE (NE, NE)	96.7 (90.2, 100.0)
12 months	NE (NE, NE)	96.7 (90.2, 100.0)
18 months	NE (NE, NE)	96.7 (90.2, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	1 (2.7)
Number of Subjects Censored, n (%)	13 (100.0)	36 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	1.1*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.527

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.2 (91.9, 100.0)
6 months	NE (NE, NE)	97.2 (91.9, 100.0)
9 months	NE (NE, NE)	97.2 (91.9, 100.0)
12 months	NE (NE, NE)	97.2 (91.9, 100.0)
18 months	NE (NE, NE)	97.2 (91.9, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	4 (10.8)
Number of Subjects Censored, n (%)	13 (100.0)	33 (89.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.68, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.242

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	91.8 (82.9, 100.0)
6 months	NE (NE, NE)	85.3 (70.4, 100.0)
9 months	NE (NE, NE)	85.3 (70.4, 100.0)
12 months	NE (NE, NE)	85.3 (70.4, 100.0)
18 months	NE (NE, NE)	85.3 (70.4, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	3 (8.1)
Number of Subjects Censored, n (%)	13 (100.0)	34 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.305

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	91.8 (82.9, 100.0)
6 months	NE (NE, NE)	91.8 (82.9, 100.0)
9 months	NE (NE, NE)	91.8 (82.9, 100.0)
12 months	NE (NE, NE)	91.8 (82.9, 100.0)
18 months	NE (NE, NE)	91.8 (82.9, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	2 (5.4)
Number of Subjects Censored, n (%)	13 (100.0)	35 (94.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	1.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.360

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.6 (87.3, 100.0)
6 months	NE (NE, NE)	94.6 (87.3, 100.0)
9 months	NE (NE, NE)	94.6 (87.3, 100.0)
12 months	NE (NE, NE)	94.6 (87.3, 100.0)
18 months	NE (NE, NE)	94.6 (87.3, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	1 (7.7)	0
Number of Subjects Censored, n (%)	12 (92.3)	37 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 5.6*	1.1*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.046

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	1.91	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	2 (15.4)	16 (43.2)
Number of Subjects Censored, n (%)	11 (84.6)	21 (56.8)
Time to first TEAE (months)		
25% percentile (95% CI)	3.71 (0.95, NE)	1.41 (0.69, 2.23)
Median (95% CI)	NE (3.71, NE)	5.78 (1.61, NE)
75% percentile (95% CI)	NE (3.71, NE)	NE (5.78, NE)
Min, Max	1.0, 3.7*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.065 (0.765)
95% CI		(0.685, 13.717)
Log-rank p-value		0.123

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	57.8 (41.4, 74.2)
6 months	NE (NE, NE)	38.5 (5.8, 71.3)
9 months	NE (NE, NE)	38.5 (5.8, 71.3)
12 months	NE (NE, NE)	38.5 (5.8, 71.3)
18 months	NE (NE, NE)	38.5 (5.8, 71.3)
Median Follow-up Time (months)	1.91	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	5 (13.5)
Number of Subjects Censored, n (%)	13 (100.0)	32 (86.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	6.87 (2.53, NE)
Median (95% CI)	NE (NE, NE)	NE (6.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (6.87, NE)
Min, Max	1.3*, 5.6*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.200

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	88.5 (77.9, 99.2)
6 months	NE (NE, NE)	88.5 (77.9, 99.2)
9 months	NE (NE, NE)	59.0 (11.3, 100.0)
12 months	NE (NE, NE)	59.0 (11.3, 100.0)
18 months	NE (NE, NE)	59.0 (11.3, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	9 (24.3)
Number of Subjects Censored, n (%)	13 (100.0)	28 (75.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.71 (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (5.78, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (5.78, NE)
Min, Max	1.3*, 5.6*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.065

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	81.0 (68.3, 93.7)
6 months	NE (NE, NE)	55.2 (21.2, 89.2)
9 months	NE (NE, NE)	55.2 (21.2, 89.2)
12 months	NE (NE, NE)	55.2 (21.2, 89.2)
18 months	NE (NE, NE)	55.2 (21.2, 89.2)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	7 (18.9)
Number of Subjects Censored, n (%)	13 (100.0)	30 (81.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.95, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.104

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	83.5 (71.5, 95.6)
6 months	NE (NE, NE)	76.6 (59.4, 93.7)
9 months	NE (NE, NE)	76.6 (59.4, 93.7)
12 months	NE (NE, NE)	76.6 (59.4, 93.7)
18 months	NE (NE, NE)	76.6 (59.4, 93.7)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	2 (5.4)
Number of Subjects Censored, n (%)	13 (100.0)	35 (94.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	1.1*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.724

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.9 (85.6, 100.0)
6 months	NE (NE, NE)	93.9 (85.6, 100.0)
9 months	NE (NE, NE)	93.9 (85.6, 100.0)
12 months	NE (NE, NE)	93.9 (85.6, 100.0)
18 months	NE (NE, NE)	93.9 (85.6, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	4 (10.8)
Number of Subjects Censored, n (%)	13 (100.0)	33 (89.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.23, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.8, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.211

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	88.2 (77.2, 99.1)
6 months	NE (NE, NE)	88.2 (77.2, 99.1)
9 months	NE (NE, NE)	88.2 (77.2, 99.1)
12 months	NE (NE, NE)	88.2 (77.2, 99.1)
18 months	NE (NE, NE)	88.2 (77.2, 99.1)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	1 (7.7)	5 (13.5)
Number of Subjects Censored, n (%)	12 (92.3)	32 (86.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.87, NE)	5.78 (1.97, NE)
Median (95% CI)	NE (NE, NE)	NE (5.78, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (5.78, NE)
Min, Max	1.3*, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.491 (1.136)
95% CI		(0.161, 13.831)
Log-rank p-value		0.933

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (73.9, 100.0)	88.6 (78.0, 99.2)
6 months	NE (NE, NE)	66.4 (28.0, 100.0)
9 months	NE (NE, NE)	66.4 (28.0, 100.0)
12 months	NE (NE, NE)	66.4 (28.0, 100.0)
18 months	NE (NE, NE)	66.4 (28.0, 100.0)
Median Follow-up Time (months)	1.91	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	4 (10.8)
Number of Subjects Censored, n (%)	13 (100.0)	33 (89.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.61, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.220

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	88.8 (78.4, 99.2)
6 months	NE (NE, NE)	88.8 (78.4, 99.2)
9 months	NE (NE, NE)	88.8 (78.4, 99.2)
12 months	NE (NE, NE)	88.8 (78.4, 99.2)
18 months	NE (NE, NE)	88.8 (78.4, 99.2)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	2 (5.4)
Number of Subjects Censored, n (%)	13 (100.0)	35 (94.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.724

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.5 (87.1, 100.0)
6 months	NE (NE, NE)	94.5 (87.1, 100.0)
9 months	NE (NE, NE)	94.5 (87.1, 100.0)
12 months	NE (NE, NE)	94.5 (87.1, 100.0)
18 months	NE (NE, NE)	94.5 (87.1, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	1 (7.7)	11 (29.7)
Number of Subjects Censored, n (%)	12 (92.3)	26 (70.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	1.87 (0.30, NE)
Median (95% CI)	NE (NE, NE)	NE (4.30, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.1, 10.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.305 (1.055)
95% CI		(0.544, 34.055)
Log-rank p-value		0.149

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	72.6 (58.1, 87.1)
6 months	NE (NE, NE)	62.2 (39.6, 84.8)
9 months	NE (NE, NE)	62.2 (39.6, 84.8)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	6 (16.2)
Number of Subjects Censored, n (%)	13 (100.0)	31 (83.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.39, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.1, 10.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.143

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	83.5 (71.4, 95.6)
6 months	NE (NE, NE)	83.5 (71.4, 95.6)
9 months	NE (NE, NE)	83.5 (71.4, 95.6)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	3 (8.1)
Number of Subjects Censored, n (%)	13 (100.0)	34 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.30, NE)
Median (95% CI)	NE (NE, NE)	NE (4.30, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.370

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.4 (86.9, 100.0)
6 months	NE (NE, NE)	82.6 (60.0, 100.0)
9 months	NE (NE, NE)	82.6 (60.0, 100.0)
12 months	NE (NE, NE)	82.6 (60.0, 100.0)
18 months	NE (NE, NE)	82.6 (60.0, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	3 (8.1)
Number of Subjects Censored, n (%)	13 (100.0)	34 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.266

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	91.6 (82.6, 100.0)
6 months	NE (NE, NE)	91.6 (82.6, 100.0)
9 months	NE (NE, NE)	91.6 (82.6, 100.0)
12 months	NE (NE, NE)	91.6 (82.6, 100.0)
18 months	NE (NE, NE)	91.6 (82.6, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	1 (7.7)	1 (2.7)
Number of Subjects Censored, n (%)	12 (92.3)	36 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.409 (1.416)
95% CI		(0.025, 6.561)
Log-rank p-value		0.486

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	97.3 (92.1, 100.0)
6 months	NE (NE, NE)	97.3 (92.1, 100.0)
9 months	NE (NE, NE)	97.3 (92.1, 100.0)
12 months	NE (NE, NE)	97.3 (92.1, 100.0)
18 months	NE (NE, NE)	97.3 (92.1, 100.0)
Median Follow-up Time (months)	1.91	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Vascular disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	1 (7.7)	9 (24.3)
Number of Subjects Censored, n (%)	12 (92.3)	28 (75.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.41, NE)	NE (0.72, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.1, 8.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.859 (1.066)
95% CI		(0.354, 23.101)
Log-rank p-value		0.394

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Vascular disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (73.9, 100.0)	75.2 (61.1, 89.3)
6 months	NE (NE, NE)	75.2 (61.1, 89.3)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	1 (7.7)	9 (24.3)
Number of Subjects Censored, n (%)	12 (92.3)	28 (75.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.41, NE)	NE (0.72, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.1, 8.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.859 (1.066)
95% CI		(0.354, 23.101)
Log-rank p-value		0.394

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (73.9, 100.0)	75.2 (61.1, 89.3)
6 months	NE (NE, NE)	75.2 (61.1, 89.3)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	4 (30.8)	8 (21.6)
Number of Subjects Censored, n (%)	9 (69.2)	29 (78.4)
Time to first TEAE (months)		
25% percentile (95% CI)	3.71 (0.03, NE)	4.70 (0.76, NE)
Median (95% CI)	NE (0.62, NE)	NE (4.70, NE)
75% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Min, Max	0.0, 3.7*	0.1, 10.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.484 (0.645)
95% CI		(0.136, 1.714)
Log-rank p-value		0.280

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.9 (54.0, 99.8)	80.4 (67.3, 93.5)
6 months	NE (NE, NE)	67.0 (40.7, 93.3)
9 months	NE (NE, NE)	67.0 (40.7, 93.3)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	5 (13.5)
Number of Subjects Censored, n (%)	13 (100.0)	32 (86.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.77, NE)
Median (95% CI)	NE (NE, NE)	NE (4.70, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.1, 10.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.276

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	88.6 (78.0, 99.1)
6 months	NE (NE, NE)	75.9 (51.2, 100.0)
9 months	NE (NE, NE)	75.9 (51.2, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	1 (2.7)
Number of Subjects Censored, n (%)	13 (100.0)	36 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.527

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.3 (92.1, 100.0)
6 months	NE (NE, NE)	97.3 (92.1, 100.0)
9 months	NE (NE, NE)	97.3 (92.1, 100.0)
12 months	NE (NE, NE)	97.3 (92.1, 100.0)
18 months	NE (NE, NE)	97.3 (92.1, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	1 (7.7)	0
Number of Subjects Censored, n (%)	12 (92.3)	37 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	3.71 (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (3.71, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Min, Max	1.3*, 3.7*	1.1*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.083

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	1 (7.7)	0
Number of Subjects Censored, n (%)	12 (92.3)	37 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.16, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 5.6*	1.1*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.046

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	1 (2.7)
Number of Subjects Censored, n (%)	13 (100.0)	36 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	6.70 (6.70, NE)
Median (95% CI)	NE (NE, NE)	NE (6.70, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (6.70, NE)
Min, Max	1.3*, 5.6*	1.1*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	66.7 (13.3, 100.0)
12 months	NE (NE, NE)	66.7 (13.3, 100.0)
18 months	NE (NE, NE)	66.7 (13.3, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	1 (2.7)
Number of Subjects Censored, n (%)	13 (100.0)	36 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.8, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.439

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.3 (92.1, 100.0)
6 months	NE (NE, NE)	97.3 (92.1, 100.0)
9 months	NE (NE, NE)	97.3 (92.1, 100.0)
12 months	NE (NE, NE)	97.3 (92.1, 100.0)
18 months	NE (NE, NE)	97.3 (92.1, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	1 (7.7)	15 (40.5)
Number of Subjects Censored, n (%)	12 (92.3)	22 (59.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	0.69 (0.26, 1.71)
Median (95% CI)	NE (NE, NE)	NE (1.15, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 3.7*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.228 (1.040)
95% CI		(0.811, 47.822)
Log-rank p-value		0.068

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	58.9 (42.8, 74.9)
6 months	NE (NE, NE)	58.9 (42.8, 74.9)
9 months	NE (NE, NE)	58.9 (42.8, 74.9)
12 months	NE (NE, NE)	58.9 (42.8, 74.9)
18 months	NE (NE, NE)	58.9 (42.8, 74.9)
Median Follow-up Time (months)	1.91	1.91

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	6 (16.2)
Number of Subjects Censored, n (%)	13 (100.0)	31 (83.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.49, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.191

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	83.8 (71.9, 95.7)
6 months	NE (NE, NE)	83.8 (71.9, 95.7)
9 months	NE (NE, NE)	83.8 (71.9, 95.7)
12 months	NE (NE, NE)	83.8 (71.9, 95.7)
18 months	NE (NE, NE)	83.8 (71.9, 95.7)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	1 (7.7)	2 (5.4)
Number of Subjects Censored, n (%)	12 (92.3)	35 (94.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 3.7*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.723 (1.247)
95% CI		(0.063, 8.323)
Log-rank p-value		0.772

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	94.3 (86.7, 100.0)
6 months	NE (NE, NE)	94.3 (86.7, 100.0)
9 months	NE (NE, NE)	94.3 (86.7, 100.0)
12 months	NE (NE, NE)	94.3 (86.7, 100.0)
18 months	NE (NE, NE)	94.3 (86.7, 100.0)
Median Follow-up Time (months)	1.91	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	1 (2.7)
Number of Subjects Censored, n (%)	13 (100.0)	36 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.540

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.3 (92.1, 100.0)
6 months	NE (NE, NE)	97.3 (92.1, 100.0)
9 months	NE (NE, NE)	97.3 (92.1, 100.0)
12 months	NE (NE, NE)	97.3 (92.1, 100.0)
18 months	NE (NE, NE)	97.3 (92.1, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	1 (7.7)	10 (27.0)
Number of Subjects Censored, n (%)	12 (92.3)	27 (73.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.20, NE)	2.40 (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.043 (1.063)
95% CI		(0.379, 24.440)
Log-rank p-value		0.355

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	70.6 (55.1, 86.2)
6 months	NE (NE, NE)	70.6 (55.1, 86.2)
9 months	NE (NE, NE)	70.6 (55.1, 86.2)
12 months	NE (NE, NE)	70.6 (55.1, 86.2)
18 months	NE (NE, NE)	70.6 (55.1, 86.2)
Median Follow-up Time (months)	2.30	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	2 (5.4)
Number of Subjects Censored, n (%)	13 (100.0)	35 (94.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.540

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.6 (87.3, 100.0)
6 months	NE (NE, NE)	94.6 (87.3, 100.0)
9 months	NE (NE, NE)	94.6 (87.3, 100.0)
12 months	NE (NE, NE)	94.6 (87.3, 100.0)
18 months	NE (NE, NE)	94.6 (87.3, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	3 (8.1)
Number of Subjects Censored, n (%)	13 (100.0)	34 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.292

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	91.8 (82.9, 100.0)
6 months	NE (NE, NE)	91.8 (82.9, 100.0)
9 months	NE (NE, NE)	91.8 (82.9, 100.0)
12 months	NE (NE, NE)	91.8 (82.9, 100.0)
18 months	NE (NE, NE)	91.8 (82.9, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	2 (5.4)
Number of Subjects Censored, n (%)	13 (100.0)	35 (94.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	1.1*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.486

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.9 (85.6, 100.0)
6 months	NE (NE, NE)	93.9 (85.6, 100.0)
9 months	NE (NE, NE)	93.9 (85.6, 100.0)
12 months	NE (NE, NE)	93.9 (85.6, 100.0)
18 months	NE (NE, NE)	93.9 (85.6, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	2 (15.4)	5 (13.5)
Number of Subjects Censored, n (%)	11 (84.6)	32 (86.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	NE (1.61, NE)
Median (95% CI)	NE (1.84, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 5.6*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.759 (0.859)
95% CI		(0.141, 4.090)
Log-rank p-value		0.742

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.1 (61.5, 100.0)	85.5 (73.7, 97.4)
6 months	NE (NE, NE)	85.5 (73.7, 97.4)
9 months	NE (NE, NE)	85.5 (73.7, 97.4)
12 months	NE (NE, NE)	85.5 (73.7, 97.4)
18 months	NE (NE, NE)	85.5 (73.7, 97.4)
Median Follow-up Time (months)	1.91	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	4 (10.8)
Number of Subjects Censored, n (%)	13 (100.0)	33 (89.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.61, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.293

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	88.9 (78.7, 99.2)
6 months	NE (NE, NE)	88.9 (78.7, 99.2)
9 months	NE (NE, NE)	88.9 (78.7, 99.2)
12 months	NE (NE, NE)	88.9 (78.7, 99.2)
18 months	NE (NE, NE)	88.9 (78.7, 99.2)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	2 (15.4)	1 (2.7)
Number of Subjects Censored, n (%)	11 (84.6)	36 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	NE (NE, NE)
Median (95% CI)	NE (1.84, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 5.6*	1.1*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.131 (1.254)
95% CI		(0.011, 1.526)
Log-rank p-value		0.064

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.1 (61.5, 100.0)	97.2 (91.9, 100.0)
6 months	NE (NE, NE)	97.2 (91.9, 100.0)
9 months	NE (NE, NE)	97.2 (91.9, 100.0)
12 months	NE (NE, NE)	97.2 (91.9, 100.0)
18 months	NE (NE, NE)	97.2 (91.9, 100.0)
Median Follow-up Time (months)	1.91	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	4 (30.8)	4 (10.8)
Number of Subjects Censored, n (%)	9 (69.2)	33 (89.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.82 (0.10, NE)	5.52 (3.71, NE)
Median (95% CI)	NE (0.76, NE)	17.48 (5.52, NE)
75% percentile (95% CI)	NE (NE, NE)	17.48 (NE, NE)
Min, Max	0.1, 3.7*	1.1*, 17.5
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.136 (0.900)
95% CI		(0.023, 0.791)
Log-rank p-value		0.029

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	69.2 (44.1, 94.3)	97.2 (91.9, 100.0)
6 months	NE (NE, NE)	74.3 (44.5, 100.0)
9 months	NE (NE, NE)	74.3 (44.5, 100.0)
12 months	NE (NE, NE)	74.3 (44.5, 100.0)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	1.91	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	1 (7.7)	1 (2.7)
Number of Subjects Censored, n (%)	12 (92.3)	36 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	4.14 (NE, NE)	NE (5.52, NE)
Median (95% CI)	4.14 (NE, NE)	NE (5.52, NE)
75% percentile (95% CI)	4.14 (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 4.1	1.1*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.157

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	0.0 (NE, NE)	83.3 (53.5, 100.0)
9 months	0.0 (NE, NE)	83.3 (53.5, 100.0)
12 months	0.0 (NE, NE)	83.3 (53.5, 100.0)
18 months	0.0 (NE, NE)	83.3 (53.5, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	1 (7.7)	0
Number of Subjects Censored, n (%)	12 (92.3)	37 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.12, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.1, 5.6*	1.1*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.197

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	2 (15.4)	3 (8.1)
Number of Subjects Censored, n (%)	11 (84.6)	34 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.0, 10.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.624 (0.917)
95% CI		(0.104, 3.764)
Log-rank p-value		0.651

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.6 (65.0, 100.0)	91.8 (82.9, 100.0)
6 months	NE (NE, NE)	91.8 (82.9, 100.0)
9 months	NE (NE, NE)	91.8 (82.9, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	1 (7.7)	2 (5.4)
Number of Subjects Censored, n (%)	12 (92.3)	35 (94.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.72, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.882 (1.227)
95% CI		(0.080, 9.777)
Log-rank p-value		0.948

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	94.5 (87.1, 100.0)
6 months	NE (NE, NE)	94.5 (87.1, 100.0)
9 months	NE (NE, NE)	94.5 (87.1, 100.0)
12 months	NE (NE, NE)	94.5 (87.1, 100.0)
18 months	NE (NE, NE)	94.5 (87.1, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	1 (7.7)	1 (2.7)
Number of Subjects Censored, n (%)	12 (92.3)	36 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.72, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.7, 10.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.482 (1.423)
95% CI		(0.030, 7.836)
Log-rank p-value		0.592

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	97.3 (92.1, 100.0)
6 months	NE (NE, NE)	97.3 (92.1, 100.0)
9 months	NE (NE, NE)	97.3 (92.1, 100.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Endocrine disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	6 (16.2)
Number of Subjects Censored, n (%)	13 (100.0)	31 (83.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.84 (1.87, NE)
Median (95% CI)	NE (NE, NE)	NE (3.84, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	1.1*, 10.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.175

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Endocrine disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	87.8 (76.5, 99.1)
6 months	NE (NE, NE)	69.0 (43.4, 94.5)
9 months	NE (NE, NE)	69.0 (43.4, 94.5)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	6 (16.2)
Number of Subjects Censored, n (%)	13 (100.0)	31 (83.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.84 (1.87, NE)
Median (95% CI)	NE (NE, NE)	NE (3.84, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	1.1*, 10.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.175

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	87.8 (76.5, 99.1)
6 months	NE (NE, NE)	69.0 (43.4, 94.5)
9 months	NE (NE, NE)	69.0 (43.4, 94.5)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	1 (7.7)	5 (13.5)
Number of Subjects Censored, n (%)	12 (92.3)	32 (86.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.87, NE)	NE (2.66, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.019 (1.097)
95% CI		(0.235, 17.323)
Log-rank p-value		0.543

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (73.9, 100.0)	87.3 (75.6, 99.1)
6 months	NE (NE, NE)	80.6 (63.9, 97.3)
9 months	NE (NE, NE)	80.6 (63.9, 97.3)
12 months	NE (NE, NE)	80.6 (63.9, 97.3)
18 months	NE (NE, NE)	80.6 (63.9, 97.3)
Median Follow-up Time (months)	1.91	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	1 (7.7)	2 (5.4)
Number of Subjects Censored, n (%)	12 (92.3)	35 (94.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.87, NE)	NE (3.25, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	1.1*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.748 (1.236)
95% CI		(0.066, 8.420)
Log-rank p-value		0.813

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (73.9, 100.0)	96.6 (89.9, 100.0)
6 months	NE (NE, NE)	90.1 (76.4, 100.0)
9 months	NE (NE, NE)	90.1 (76.4, 100.0)
12 months	NE (NE, NE)	90.1 (76.4, 100.0)
18 months	NE (NE, NE)	90.1 (76.4, 100.0)
Median Follow-up Time (months)	1.91	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	1 (2.7)
Number of Subjects Censored, n (%)	13 (100.0)	36 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.540

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.3 (92.1, 100.0)
6 months	NE (NE, NE)	97.3 (92.1, 100.0)
9 months	NE (NE, NE)	97.3 (92.1, 100.0)
12 months	NE (NE, NE)	97.3 (92.1, 100.0)
18 months	NE (NE, NE)	97.3 (92.1, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	1 (2.7)
Number of Subjects Censored, n (%)	13 (100.0)	36 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 5.6*	1.1*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.527

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.2 (91.9, 100.0)
6 months	NE (NE, NE)	97.2 (91.9, 100.0)
9 months	NE (NE, NE)	97.2 (91.9, 100.0)
12 months	NE (NE, NE)	97.2 (91.9, 100.0)
18 months	NE (NE, NE)	97.2 (91.9, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	2 (5.4)
Number of Subjects Censored, n (%)	13 (100.0)	35 (94.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	7.62 (3.75, NE)
Median (95% CI)	NE (NE, NE)	NE (7.62, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (7.62, NE)
Min, Max	1.3*, 5.6*	1.1*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.527

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	90.9 (73.9, 100.0)
9 months	NE (NE, NE)	60.6 (10.8, 100.0)
12 months	NE (NE, NE)	60.6 (10.8, 100.0)
18 months	NE (NE, NE)	60.6 (10.8, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Number of Subjects with Events, n (%)	0	1 (2.7)
Number of Subjects Censored, n (%)	13 (100.0)	36 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	7.62 (7.62, NE)
Median (95% CI)	NE (NE, NE)	NE (7.62, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (7.62, NE)
Min, Max	1.3*, 5.6*	1.1*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
<= 18 months

Statistics	Placebo + BSC N=13	Fruquintinib + BSC N=37
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	66.7 (13.3, 100.0)
12 months	NE (NE, NE)	66.7 (13.3, 100.0)
18 months	NE (NE, NE)	66.7 (13.3, 100.0)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	125 (57.6)	293 (69.9)
Number of Subjects Censored, n (%)	92 (42.4)	126 (30.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.46, 0.69)	0.36 (0.30, 0.59)
Median (95% CI)	1.64 (1.25, 2.76)	1.18 (0.92, 1.61)
75% percentile (95% CI)	NE (NE, NE)	6.47 (4.47, NE)
Min, Max	0.0, 13.0*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.206 (0.109)
95% CI		(0.975, 1.492)
Log-rank p-value		0.111

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	41.9 (35.1, 48.7)	37.6 (32.8, 42.3)
6 months	35.2 (25.4, 45.1)	25.1 (20.2, 30.0)
9 months	35.2 (25.4, 45.1)	19.9 (14.3, 25.6)
12 months	35.2 (25.4, 45.1)	19.9 (14.3, 25.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.61	1.12

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	51 (23.5)	144 (34.4)
Number of Subjects Censored, n (%)	166 (76.5)	275 (65.6)
Time to first TEAE (months)		
25% percentile (95% CI)	3.22 (0.95, NE)	1.18 (0.89, 1.74)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.352 (0.164)
95% CI		(0.981, 1.865)
Log-rank p-value		0.064

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.2 (70.3, 82.1)	67.6 (63.1, 72.2)
6 months	69.7 (58.8, 80.6)	63.5 (58.5, 68.5)
9 months	69.7 (58.8, 80.6)	60.9 (54.8, 67.0)
12 months	69.7 (58.8, 80.6)	60.9 (54.8, 67.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	35 (16.1)	87 (20.8)
Number of Subjects Censored, n (%)	182 (83.9)	332 (79.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.71, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.232 (0.205)
95% CI		(0.824, 1.842)
Log-rank p-value		0.336

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.7 (77.5, 88.0)	80.8 (77.0, 84.7)
6 months	82.7 (77.5, 88.0)	77.6 (73.2, 82.0)
9 months	82.7 (77.5, 88.0)	75.5 (70.3, 80.7)
12 months	82.7 (77.5, 88.0)	75.5 (70.3, 80.7)
18 months	NE (NE, NE)	75.5 (70.3, 80.7)
Median Follow-up Time (months)	2.60	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	23 (10.6)	43 (10.3)
Number of Subjects Censored, n (%)	194 (89.4)	376 (89.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.70, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.768 (0.264)
95% CI		(0.457, 1.289)
Log-rank p-value		0.294

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.8 (84.3, 93.3)	91.6 (88.9, 94.3)
6 months	83.8 (73.5, 94.1)	88.9 (85.4, 92.3)
9 months	83.8 (73.5, 94.1)	87.4 (83.4, 91.3)
12 months	83.8 (73.5, 94.1)	82.5 (72.5, 92.5)
18 months	NE (NE, NE)	82.5 (72.5, 92.5)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	6 (2.8)	58 (13.8)
Number of Subjects Censored, n (%)	211 (97.2)	361 (86.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
Median (95% CI)	NE (NE, NE)	NE (13.24, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.24, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.888 (0.436)
95% CI		(2.080, 11.489)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.0 (94.7, 99.4)	87.6 (84.4, 90.8)
6 months	97.0 (94.7, 99.4)	85.8 (82.2, 89.4)
9 months	97.0 (94.7, 99.4)	83.6 (78.9, 88.2)
12 months	97.0 (94.7, 99.4)	83.6 (78.9, 88.2)
18 months	NE (NE, NE)	55.7 (11.0, 100.0)
Median Follow-up Time (months)	2.83	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	28 (12.9)	23 (5.5)
Number of Subjects Censored, n (%)	189 (87.1)	396 (94.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.271 (0.295)
95% CI		(0.152, 0.483)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.5 (81.6, 91.4)	96.4 (94.6, 98.3)
6 months	82.8 (75.8, 89.8)	92.7 (89.6, 95.9)
9 months	82.8 (75.8, 89.8)	92.7 (89.6, 95.9)
12 months	82.8 (75.8, 89.8)	92.7 (89.6, 95.9)
18 months	NE (NE, NE)	86.1 (73.3, 98.9)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	17 (7.8)	21 (5.0)
Number of Subjects Censored, n (%)	200 (92.2)	398 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.533 (0.333)
95% CI		(0.277, 1.023)
Log-rank p-value		0.052

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.7 (87.8, 95.5)	95.3 (93.2, 97.3)
6 months	91.7 (87.8, 95.5)	95.3 (93.2, 97.3)
9 months	91.7 (87.8, 95.5)	93.2 (88.7, 97.7)
12 months	91.7 (87.8, 95.5)	90.2 (82.9, 97.4)
18 months	NE (NE, NE)	90.2 (82.9, 97.4)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	4 (1.8)	16 (3.8)
Number of Subjects Censored, n (%)	213 (98.2)	403 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.185 (0.584)
95% CI		(0.377, 3.724)
Log-rank p-value		0.820

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (96.3, 99.9)	98.0 (96.6, 99.4)
6 months	98.1 (96.3, 99.9)	96.2 (94.0, 98.4)
9 months	98.1 (96.3, 99.9)	94.9 (91.6, 98.3)
12 months	98.1 (96.3, 99.9)	87.3 (78.4, 96.2)
18 months	NE (NE, NE)	87.3 (78.4, 96.2)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	4 (1.8)	11 (2.6)
Number of Subjects Censored, n (%)	213 (98.2)	408 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.960 (0.598)
95% CI		(0.298, 3.099)
Log-rank p-value		0.893

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (95.3, 100.0)	97.9 (96.4, 99.3)
6 months	97.7 (95.3, 100.0)	96.9 (95.0, 98.9)
9 months	97.7 (95.3, 100.0)	95.6 (92.4, 98.8)
12 months	97.7 (95.3, 100.0)	95.6 (92.4, 98.8)
18 months	NE (NE, NE)	95.6 (92.4, 98.8)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	2 (0.9)	11 (2.6)
Number of Subjects Censored, n (%)	215 (99.1)	408 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.240 (0.783)
95% CI		(0.483, 10.389)
Log-rank p-value		0.270

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.8, 100.0)	98.1 (96.7, 99.4)
6 months	99.1 (97.8, 100.0)	96.9 (94.8, 99.0)
9 months	99.1 (97.8, 100.0)	95.0 (90.8, 99.2)
12 months	99.1 (97.8, 100.0)	95.0 (90.8, 99.2)
18 months	NE (NE, NE)	95.0 (90.8, 99.2)
Median Follow-up Time (months)	2.83	4.11

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	122 (56.2)	292 (69.7)
Number of Subjects Censored, n (%)	95 (43.8)	127 (30.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.62 (0.43, 0.69)	0.49 (0.39, 0.66)
Median (95% CI)	1.68 (1.31, 2.92)	1.38 (0.95, 1.84)
75% percentile (95% CI)	5.59 (4.34, NE)	5.55 (4.63, 7.79)
Min, Max	0.0, 6.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.133 (0.110)
95% CI		(0.913, 1.406)
Log-rank p-value		0.274

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	41.9 (34.6, 49.3)	37.2 (32.4, 41.9)
6 months	20.4 (4.6, 36.3)	24.0 (18.8, 29.2)
9 months	NE (NE, NE)	18.1 (12.4, 23.8)
12 months	NE (NE, NE)	15.5 (8.8, 22.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.38	1.28

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	24 (11.1)	107 (25.5)
Number of Subjects Censored, n (%)	193 (88.9)	312 (74.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.96 (2.33, 6.47)
Median (95% CI)	NE (NE, NE)	NE (10.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.087 (0.232)
95% CI		(1.324, 3.290)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.6 (84.2, 92.9)	77.8 (73.7, 81.9)
6 months	88.6 (84.2, 92.9)	71.1 (65.8, 76.4)
9 months	88.6 (84.2, 92.9)	67.3 (61.0, 73.5)
12 months	88.6 (84.2, 92.9)	61.7 (49.7, 73.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	2.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	40 (18.4)	76 (18.1)
Number of Subjects Censored, n (%)	177 (81.6)	343 (81.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	9.00 (5.55, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.753 (0.202)
95% CI		(0.507, 1.118)
Log-rank p-value		0.170

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.1 (75.7, 86.5)	84.4 (80.8, 88.1)
6 months	77.7 (69.5, 86.0)	79.1 (74.4, 83.8)
9 months	77.7 (69.5, 86.0)	76.2 (70.5, 81.8)
12 months	77.7 (69.5, 86.0)	72.2 (64.5, 79.8)
18 months	NE (NE, NE)	72.2 (64.5, 79.8)
Median Follow-up Time (months)	2.76	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	32 (14.7)	77 (18.4)
Number of Subjects Censored, n (%)	185 (85.3)	342 (81.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	9.23 (5.52, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.940 (0.217)
95% CI		(0.615, 1.437)
Log-rank p-value		0.818

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.2 (77.5, 88.9)	84.6 (81.0, 88.3)
6 months	83.2 (77.5, 88.9)	79.9 (75.4, 84.4)
9 months	83.2 (77.5, 88.9)	75.1 (69.1, 81.1)
12 months	83.2 (77.5, 88.9)	70.2 (61.4, 78.9)
18 months	NE (NE, NE)	70.2 (61.4, 78.9)
Median Follow-up Time (months)	2.79	3.42

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	22 (10.1)	76 (18.1)
Number of Subjects Censored, n (%)	195 (89.9)	343 (81.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	9.33 (5.62, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.339 (0.246)
95% CI		(0.826, 2.170)
Log-rank p-value		0.237

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.7 (83.6, 93.7)	84.6 (81.0, 88.3)
6 months	87.0 (81.1, 92.9)	78.9 (74.2, 83.6)
9 months	87.0 (81.1, 92.9)	75.8 (70.2, 81.5)
12 months	87.0 (81.1, 92.9)	73.6 (66.6, 80.6)
18 months	NE (NE, NE)	73.6 (66.6, 80.6)
Median Follow-up Time (months)	2.79	3.52

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	26 (12.0)	63 (15.0)
Number of Subjects Censored, n (%)	191 (88.0)	356 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.36, NE)	10.18 (7.10, NE)
Median (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.884 (0.241)
95% CI		(0.551, 1.417)
Log-rank p-value		0.651

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.0 (83.4, 92.5)	88.7 (85.6, 91.8)
6 months	80.8 (69.6, 92.0)	83.2 (78.9, 87.6)
9 months	80.8 (69.6, 92.0)	79.6 (74.1, 85.1)
12 months	80.8 (69.6, 92.0)	74.8 (66.6, 83.1)
18 months	NE (NE, NE)	74.8 (66.6, 83.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	8 (3.7)	62 (14.8)
Number of Subjects Censored, n (%)	209 (96.3)	357 (85.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.750 (0.377)
95% CI		(1.790, 7.854)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.0 (93.2, 98.7)	86.6 (83.3, 89.9)
6 months	96.0 (93.2, 98.7)	84.2 (80.4, 88.1)
9 months	96.0 (93.2, 98.7)	82.0 (77.2, 86.8)
12 months	96.0 (93.2, 98.7)	82.0 (77.2, 86.8)
18 months	NE (NE, NE)	82.0 (77.2, 86.8)
Median Follow-up Time (months)	2.83	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	8 (3.7)	31 (7.4)
Number of Subjects Censored, n (%)	209 (96.3)	388 (92.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.468 (0.406)
95% CI		(0.662, 3.255)
Log-rank p-value		0.338

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.6 (94.1, 99.1)	94.0 (91.7, 96.4)
6 months	90.2 (77.7, 100.0)	91.1 (87.9, 94.4)
9 months	NE (NE, NE)	89.8 (85.7, 93.9)
12 months	NE (NE, NE)	89.8 (85.7, 93.9)
18 months	NE (NE, NE)	89.8 (85.7, 93.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	4 (1.8)	15 (3.6)
Number of Subjects Censored, n (%)	213 (98.2)	404 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.621 (0.572)
95% CI		(0.529, 4.971)
Log-rank p-value		0.376

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (96.1, 99.9)	97.1 (95.5, 98.7)
6 months	98.0 (96.1, 99.9)	95.9 (93.7, 98.2)
9 months	98.0 (96.1, 99.9)	94.7 (91.3, 98.0)
12 months	98.0 (96.1, 99.9)	94.7 (91.3, 98.0)
18 months	NE (NE, NE)	94.7 (91.3, 98.0)
Median Follow-up Time (months)	2.83	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	4 (1.8)	10 (2.4)
Number of Subjects Censored, n (%)	213 (98.2)	409 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.910 (0.614)
95% CI		(0.273, 3.033)
Log-rank p-value		0.959

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.9 (95.8, 100.0)	97.5 (95.9, 99.0)
6 months	97.9 (95.8, 100.0)	97.5 (95.9, 99.0)
9 months	97.9 (95.8, 100.0)	97.5 (95.9, 99.0)
12 months	97.9 (95.8, 100.0)	97.5 (95.9, 99.0)
18 months	NE (NE, NE)	97.5 (95.9, 99.0)
Median Follow-up Time (months)	2.83	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	10 (4.6)	3 (0.7)
Number of Subjects Censored, n (%)	207 (95.4)	416 (99.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.115 (0.685)
95% CI		(0.030, 0.440)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.0 (91.9, 98.0)	99.5 (98.8, 100.0)
6 months	95.0 (91.9, 98.0)	98.8 (97.2, 100.0)
9 months	95.0 (91.9, 98.0)	98.8 (97.2, 100.0)
12 months	95.0 (91.9, 98.0)	98.8 (97.2, 100.0)
18 months	NE (NE, NE)	98.8 (97.2, 100.0)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	0	13 (3.1)
Number of Subjects Censored, n (%)	217 (100.0)	406 (96.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.014

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.9 (95.2, 98.7)
6 months	100.0 (100.0, 100.0)	96.9 (95.2, 98.7)
9 months	100.0 (100.0, 100.0)	95.5 (92.3, 98.8)
12 months	100.0 (100.0, 100.0)	95.5 (92.3, 98.8)
18 months	NE (NE, NE)	95.5 (92.3, 98.8)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	61 (28.1)	184 (43.9)
Number of Subjects Censored, n (%)	156 (71.9)	235 (56.1)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.92, NE)	1.31 (0.95, 1.61)
Median (95% CI)	10.18 (NE, NE)	6.28 (4.73, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.0, 10.2	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.368 (0.150)
95% CI		(1.019, 1.837)
Log-rank p-value		0.039

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.9 (65.7, 78.1)	59.5 (54.6, 64.4)
6 months	66.8 (57.6, 76.0)	52.5 (47.0, 58.0)
9 months	66.8 (57.6, 76.0)	47.8 (41.5, 54.1)
12 months	0.0 (NE, NE)	45.4 (37.9, 52.9)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.53	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	39 (18.0)	121 (28.9)
Number of Subjects Censored, n (%)	178 (82.0)	298 (71.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.27, NE)	2.76 (1.71, 3.94)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.428 (0.188)
95% CI		(0.988, 2.064)
Log-rank p-value		0.063

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.4 (76.1, 86.8)	72.7 (68.3, 77.2)
6 months	78.3 (70.4, 86.2)	68.8 (63.8, 73.7)
9 months	78.3 (70.4, 86.2)	66.4 (60.9, 71.8)
12 months	78.3 (70.4, 86.2)	64.2 (57.4, 71.0)
18 months	NE (NE, NE)	64.2 (57.4, 71.0)
Median Follow-up Time (months)	2.79	2.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	4 (1.8)	27 (6.4)
Number of Subjects Censored, n (%)	213 (98.2)	392 (93.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.6*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.698 (0.540)
95% CI		(0.935, 7.780)
Log-rank p-value		0.051

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (96.3, 99.9)	93.7 (91.3, 96.2)
6 months	98.1 (96.3, 99.9)	92.9 (90.1, 95.6)
9 months	98.1 (96.3, 99.9)	91.6 (87.9, 95.2)
12 months	98.1 (96.3, 99.9)	91.6 (87.9, 95.2)
18 months	NE (NE, NE)	91.6 (87.9, 95.2)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	5 (2.3)	19 (4.5)
Number of Subjects Censored, n (%)	212 (97.7)	400 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.329 (0.514)
95% CI		(0.485, 3.641)
Log-rank p-value		0.529

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (96.3, 99.9)	96.4 (94.6, 98.3)
6 months	96.3 (92.2, 100.0)	94.3 (91.6, 97.1)
9 months	96.3 (92.2, 100.0)	93.2 (89.6, 96.7)
12 months	96.3 (92.2, 100.0)	93.2 (89.6, 96.7)
18 months	NE (NE, NE)	93.2 (89.6, 96.7)
Median Follow-up Time (months)	2.83	4.07

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	4 (1.8)	10 (2.4)
Number of Subjects Censored, n (%)	213 (98.2)	409 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.035 (0.601)
95% CI		(0.318, 3.362)
Log-rank p-value		0.958

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (95.9, 100.0)	97.7 (96.2, 99.2)
6 months	98.0 (95.9, 100.0)	97.7 (96.2, 99.2)
9 months	98.0 (95.9, 100.0)	95.8 (92.0, 99.7)
12 months	98.0 (95.9, 100.0)	95.8 (92.0, 99.7)
18 months	NE (NE, NE)	95.8 (92.0, 99.7)
Median Follow-up Time (months)	2.83	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	3 (1.4)	12 (2.9)
Number of Subjects Censored, n (%)	214 (98.6)	407 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.609 (0.655)
95% CI		(0.446, 5.809)
Log-rank p-value		0.426

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (97.0, 100.0)	97.4 (95.8, 99.0)
6 months	98.6 (97.0, 100.0)	96.7 (94.7, 98.8)
9 months	98.6 (97.0, 100.0)	95.5 (92.4, 98.6)
12 months	98.6 (97.0, 100.0)	95.5 (92.4, 98.6)
18 months	NE (NE, NE)	95.5 (92.4, 98.6)
Median Follow-up Time (months)	2.83	4.11

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	0	18 (4.3)
Number of Subjects Censored, n (%)	217 (100.0)	401 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.008

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.5 (94.7, 98.3)
6 months	100.0 (100.0, 100.0)	94.9 (92.3, 97.5)
9 months	100.0 (100.0, 100.0)	93.7 (90.4, 97.1)
12 months	100.0 (100.0, 100.0)	93.7 (90.4, 97.1)
18 months	NE (NE, NE)	93.7 (90.4, 97.1)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	3 (1.4)	11 (2.6)
Number of Subjects Censored, n (%)	214 (98.6)	408 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.511 (0.658)
95% CI		(0.416, 5.483)
Log-rank p-value		0.540

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (96.0, 100.0)	97.4 (95.8, 99.0)
6 months	98.2 (96.0, 100.0)	97.4 (95.8, 99.0)
9 months	98.2 (96.0, 100.0)	96.6 (94.4, 98.8)
12 months	98.2 (96.0, 100.0)	96.6 (94.4, 98.8)
18 months	NE (NE, NE)	96.6 (94.4, 98.8)
Median Follow-up Time (months)	2.83	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	2 (0.9)	13 (3.1)
Number of Subjects Censored, n (%)	215 (99.1)	406 (96.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.368 (0.772)
95% CI		(0.521, 10.753)
Log-rank p-value		0.228

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.8, 100.0)	97.7 (96.3, 99.2)
6 months	99.1 (97.8, 100.0)	96.7 (94.6, 98.8)
9 months	99.1 (97.8, 100.0)	94.1 (89.8, 98.4)
12 months	99.1 (97.8, 100.0)	94.1 (89.8, 98.4)
18 months	NE (NE, NE)	94.1 (89.8, 98.4)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	2 (0.9)	11 (2.6)
Number of Subjects Censored, n (%)	215 (99.1)	408 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Median (95% CI)	10.18 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 10.2	0.6*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.259 (0.781)
95% CI		(0.489, 10.447)
Log-rank p-value		0.311

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.6, 100.0)	97.2 (95.6, 98.8)
6 months	99.5 (98.6, 100.0)	97.2 (95.6, 98.8)
9 months	99.5 (98.6, 100.0)	97.2 (95.6, 98.8)
12 months	0.0 (NE, NE)	97.2 (95.6, 98.8)
18 months	0.0 (NE, NE)	97.2 (95.6, 98.8)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	1 (0.5)	11 (2.6)
Number of Subjects Censored, n (%)	216 (99.5)	408 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.748 (1.065)
95% CI		(0.341, 22.143)
Log-rank p-value		0.293

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.4, 100.0)	98.6 (97.4, 99.8)
6 months	99.5 (98.4, 100.0)	95.4 (92.6, 98.2)
9 months	99.5 (98.4, 100.0)	95.4 (92.6, 98.2)
12 months	99.5 (98.4, 100.0)	95.4 (92.6, 98.2)
18 months	NE (NE, NE)	95.4 (92.6, 98.2)
Median Follow-up Time (months)	2.83	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	61 (28.1)	170 (40.6)
Number of Subjects Censored, n (%)	156 (71.9)	249 (59.4)
Time to first TEAE (months)		
25% percentile (95% CI)	1.77 (0.95, 5.59)	1.61 (0.99, 1.84)
Median (95% CI)	NE (5.82, NE)	7.85 (6.05, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (16.79, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.213 (0.152)
95% CI		(0.901, 1.632)
Log-rank p-value		0.201

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.6 (65.3, 77.9)	63.5 (58.8, 68.3)
6 months	54.9 (35.3, 74.5)	56.5 (51.0, 62.1)
9 months	NE (NE, NE)	49.0 (42.3, 55.8)
12 months	NE (NE, NE)	49.0 (42.3, 55.8)
18 months	NE (NE, NE)	32.7 (6.1, 59.2)
Median Follow-up Time (months)	2.69	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	21 (9.7)	51 (12.2)
Number of Subjects Censored, n (%)	196 (90.3)	368 (87.8)
Time to first TEAE (months)		
25% percentile (95% CI)	5.82 (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.82, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.949 (0.266)
95% CI		(0.563, 1.598)
Log-rank p-value		0.857

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.3 (84.6, 93.9)	89.4 (86.3, 92.4)
6 months	72.9 (51.1, 94.7)	85.6 (81.6, 89.7)
9 months	NE (NE, NE)	83.6 (78.7, 88.5)
12 months	NE (NE, NE)	83.6 (78.7, 88.5)
18 months	NE (NE, NE)	83.6 (78.7, 88.5)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	11 (5.1)	39 (9.3)
Number of Subjects Censored, n (%)	206 (94.9)	380 (90.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.368 (0.349)
95% CI		(0.691, 2.709)
Log-rank p-value		0.324

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.2 (92.3, 98.1)	91.7 (88.9, 94.5)
6 months	88.9 (76.6, 100.0)	89.7 (86.4, 93.1)
9 months	NE (NE, NE)	87.0 (82.4, 91.5)
12 months	NE (NE, NE)	87.0 (82.4, 91.5)
18 months	NE (NE, NE)	87.0 (82.4, 91.5)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	9 (4.1)	40 (9.5)
Number of Subjects Censored, n (%)	208 (95.9)	379 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.708 (0.376)
95% CI		(0.818, 3.566)
Log-rank p-value		0.143

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.2 (93.6, 98.8)	92.1 (89.4, 94.8)
6 months	89.8 (77.4, 100.0)	89.6 (86.2, 93.0)
9 months	NE (NE, NE)	86.0 (81.2, 90.8)
12 months	NE (NE, NE)	86.0 (81.2, 90.8)
18 months	NE (NE, NE)	86.0 (81.2, 90.8)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	11 (5.1)	34 (8.1)
Number of Subjects Censored, n (%)	206 (94.9)	385 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.205 (0.353)
95% CI		(0.604, 2.407)
Log-rank p-value		0.631

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.8 (91.8, 97.8)	93.7 (91.3, 96.1)
6 months	94.8 (91.8, 97.8)	90.5 (87.2, 93.8)
9 months	94.8 (91.8, 97.8)	88.5 (84.3, 92.8)
12 months	94.8 (91.8, 97.8)	88.5 (84.3, 92.8)
18 months	NE (NE, NE)	88.5 (84.3, 92.8)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	3 (1.4)	28 (6.7)
Number of Subjects Censored, n (%)	214 (98.6)	391 (93.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.589 (0.613)
95% CI		(1.080, 11.928)
Log-rank p-value		0.030

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (97.3, 100.0)	94.1 (91.8, 96.4)
6 months	96.4 (91.4, 100.0)	92.8 (89.9, 95.7)
9 months	96.4 (91.4, 100.0)	89.5 (84.5, 94.4)
12 months	96.4 (91.4, 100.0)	89.5 (84.5, 94.4)
18 months	NE (NE, NE)	89.5 (84.5, 94.4)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	9 (4.1)	19 (4.5)
Number of Subjects Censored, n (%)	208 (95.9)	400 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.5, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.867 (0.412)
95% CI		(0.387, 1.943)
Log-rank p-value		0.746

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (92.4, 98.4)	96.0 (94.0, 97.9)
6 months	95.4 (92.4, 98.4)	94.9 (92.5, 97.3)
9 months	95.4 (92.4, 98.4)	94.2 (91.4, 97.0)
12 months	95.4 (92.4, 98.4)	94.2 (91.4, 97.0)
18 months	NE (NE, NE)	94.2 (91.4, 97.0)
Median Follow-up Time (months)	2.83	3.98

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	2 (0.9)	23 (5.5)
Number of Subjects Censored, n (%)	215 (99.1)	396 (94.5)
Time to first TEAE (months)		
25% percentile (95% CI)	7.43 (7.43, NE)	NE (NE, NE)
Median (95% CI)	7.43 (7.43, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (7.43, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.5, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.667 (0.741)
95% CI		(1.092, 19.941)
Log-rank p-value		0.022

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.6, 100.0)	94.9 (92.7, 97.1)
6 months	99.5 (98.6, 100.0)	93.4 (90.7, 96.2)
9 months	NE (NE, NE)	93.4 (90.7, 96.2)
12 months	NE (NE, NE)	93.4 (90.7, 96.2)
18 months	NE (NE, NE)	93.4 (90.7, 96.2)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	5 (2.3)	18 (4.3)
Number of Subjects Censored, n (%)	212 (97.7)	401 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.322 (0.514)
95% CI		(0.482, 3.623)
Log-rank p-value		0.573

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.6, 100.0)	96.3 (94.4, 98.2)
6 months	95.4 (90.3, 100.0)	94.7 (92.1, 97.3)
9 months	95.4 (90.3, 100.0)	94.0 (91.0, 97.0)
12 months	95.4 (90.3, 100.0)	94.0 (91.0, 97.0)
18 months	NE (NE, NE)	94.0 (91.0, 97.0)
Median Follow-up Time (months)	2.83	3.98

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	1 (0.5)	13 (3.1)
Number of Subjects Censored, n (%)	216 (99.5)	406 (96.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.996 (1.044)
95% CI		(0.646, 38.642)
Log-rank p-value		0.089

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.6, 100.0)	97.1 (95.3, 98.8)
6 months	99.5 (98.6, 100.0)	96.5 (94.6, 98.5)
9 months	99.5 (98.6, 100.0)	95.5 (92.7, 98.3)
12 months	99.5 (98.6, 100.0)	95.5 (92.7, 98.3)
18 months	NE (NE, NE)	95.5 (92.7, 98.3)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	2 (0.9)	11 (2.6)
Number of Subjects Censored, n (%)	215 (99.1)	408 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.297 (0.775)
95% CI		(0.503, 10.485)
Log-rank p-value		0.268

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.7, 100.0)	97.4 (95.8, 99.0)
6 months	99.0 (97.7, 100.0)	97.4 (95.8, 99.0)
9 months	99.0 (97.7, 100.0)	96.4 (93.8, 98.9)
12 months	99.0 (97.7, 100.0)	96.4 (93.8, 98.9)
18 months	NE (NE, NE)	96.4 (93.8, 98.9)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	56 (25.8)	164 (39.1)
Number of Subjects Censored, n (%)	161 (74.2)	255 (60.9)
Time to first TEAE (months)		
25% percentile (95% CI)	2.04 (1.25, NE)	0.72 (0.69, 1.45)
Median (95% CI)	NE (NE, NE)	11.53 (7.56, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.476 (0.158)
95% CI		(1.083, 2.011)
Log-rank p-value		0.016

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.4 (66.2, 78.7)	64.5 (59.9, 69.2)
6 months	72.4 (66.2, 78.7)	59.3 (54.0, 64.5)
9 months	72.4 (66.2, 78.7)	55.9 (50.0, 61.9)
12 months	72.4 (66.2, 78.7)	47.7 (37.2, 58.1)
18 months	NE (NE, NE)	47.7 (37.2, 58.1)
Median Follow-up Time (months)	2.40	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	12 (5.5)	68 (16.2)
Number of Subjects Censored, n (%)	205 (94.5)	351 (83.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.073 (0.314)
95% CI		(1.659, 5.691)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.0 (90.7, 97.3)	83.8 (80.2, 87.3)
6 months	94.0 (90.7, 97.3)	83.4 (79.7, 87.0)
9 months	94.0 (90.7, 97.3)	83.4 (79.7, 87.0)
12 months	94.0 (90.7, 97.3)	83.4 (79.7, 87.0)
18 months	NE (NE, NE)	83.4 (79.7, 87.0)
Median Follow-up Time (months)	2.83	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	22 (10.1)	40 (9.5)
Number of Subjects Censored, n (%)	195 (89.9)	379 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	14.32 (14.32, NE)
Median (95% CI)	NE (NE, NE)	NE (14.32, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.744 (0.277)
95% CI		(0.432, 1.282)
Log-rank p-value		0.288

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.4 (85.2, 93.6)	92.2 (89.6, 94.9)
6 months	89.4 (85.2, 93.6)	89.9 (86.5, 93.2)
9 months	89.4 (85.2, 93.6)	88.4 (84.6, 92.2)
12 months	89.4 (85.2, 93.6)	85.1 (77.8, 92.4)
18 months	NE (NE, NE)	68.1 (37.7, 98.5)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	21 (9.7)	35 (8.4)
Number of Subjects Censored, n (%)	196 (90.3)	384 (91.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.741 (0.286)
95% CI		(0.423, 1.299)
Log-rank p-value		0.302

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.7 (85.4, 93.9)	92.3 (89.7, 94.9)
6 months	89.7 (85.4, 93.9)	91.4 (88.5, 94.3)
9 months	89.7 (85.4, 93.9)	90.6 (87.4, 93.9)
12 months	89.7 (85.4, 93.9)	85.6 (75.5, 95.7)
18 months	NE (NE, NE)	85.6 (75.5, 95.7)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	2 (0.9)	17 (4.1)
Number of Subjects Censored, n (%)	215 (99.1)	402 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.034 (0.748)
95% CI		(0.932, 17.468)
Log-rank p-value		0.047

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.8, 100.0)	95.7 (93.7, 97.7)
6 months	99.1 (97.8, 100.0)	95.7 (93.7, 97.7)
9 months	99.1 (97.8, 100.0)	95.7 (93.7, 97.7)
12 months	99.1 (97.8, 100.0)	95.7 (93.7, 97.7)
18 months	NE (NE, NE)	95.7 (93.7, 97.7)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	2 (0.9)	10 (2.4)
Number of Subjects Censored, n (%)	215 (99.1)	409 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.612 (0.805)
95% CI		(0.333, 7.810)
Log-rank p-value		0.572

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.5, 100.0)	98.3 (97.1, 99.6)
6 months	99.0 (97.5, 100.0)	97.7 (96.0, 99.4)
9 months	99.0 (97.5, 100.0)	95.9 (92.9, 98.9)
12 months	99.0 (97.5, 100.0)	95.9 (92.9, 98.9)
18 months	NE (NE, NE)	95.9 (92.9, 98.9)
Median Follow-up Time (months)	2.83	4.11

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Vascular disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	33 (15.2)	170 (40.6)
Number of Subjects Censored, n (%)	184 (84.8)	249 (59.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.61, NE)	0.85 (0.69, 1.18)
Median (95% CI)	NE (NE, NE)	NE (6.93, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.884 (0.194)
95% CI		(1.973, 4.217)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Vascular disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.1 (79.0, 89.2)	60.7 (55.9, 65.5)
6 months	81.4 (74.2, 88.6)	57.0 (51.7, 62.3)
9 months	NE (NE, NE)	52.6 (46.1, 59.0)
12 months	NE (NE, NE)	52.6 (46.1, 59.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	2.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	19 (8.8)	159 (37.9)
Number of Subjects Censored, n (%)	198 (91.2)	260 (62.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.95 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	NE (7.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.618 (0.244)
95% CI		(2.864, 7.447)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.5 (86.3, 94.6)	63.2 (58.4, 67.9)
6 months	90.5 (86.3, 94.6)	60.7 (55.6, 65.7)
9 months	NE (NE, NE)	55.1 (48.5, 61.7)
12 months	NE (NE, NE)	55.1 (48.5, 61.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	44 (20.3)	145 (34.6)
Number of Subjects Censored, n (%)	173 (79.7)	274 (65.4)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (2.53, NE)	1.61 (0.99, 2.17)
Median (95% CI)	NE (NE, NE)	NE (8.64, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.606 (0.175)
95% CI		(1.138, 2.265)
Log-rank p-value		0.007

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.9 (73.1, 84.7)	67.3 (62.7, 71.9)
6 months	68.7 (53.0, 84.4)	62.8 (57.6, 68.1)
9 months	NE (NE, NE)	57.4 (50.2, 64.6)
12 months	NE (NE, NE)	54.6 (45.8, 63.3)
18 months	NE (NE, NE)	54.6 (45.8, 63.3)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	17 (7.8)	42 (10.0)
Number of Subjects Censored, n (%)	200 (92.2)	377 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.032 (0.291)
95% CI		(0.583, 1.825)
Log-rank p-value		0.806

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.8 (88.1, 95.6)	90.8 (87.9, 93.7)
6 months	91.8 (88.1, 95.6)	88.4 (85.0, 91.9)
9 months	91.8 (88.1, 95.6)	87.7 (84.0, 91.5)
12 months	91.8 (88.1, 95.6)	87.7 (84.0, 91.5)
18 months	NE (NE, NE)	87.7 (84.0, 91.5)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	10 (4.6)	49 (11.7)
Number of Subjects Censored, n (%)	207 (95.4)	370 (88.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.077 (0.352)
95% CI		(1.043, 4.138)
Log-rank p-value		0.037

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (92.8, 98.4)	89.8 (86.8, 92.8)
6 months	89.3 (76.9, 100.0)	87.1 (83.3, 90.9)
9 months	NE (NE, NE)	83.4 (78.0, 88.9)
12 months	NE (NE, NE)	83.4 (78.0, 88.9)
18 months	NE (NE, NE)	83.4 (78.0, 88.9)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	4 (1.8)	26 (6.2)
Number of Subjects Censored, n (%)	213 (98.2)	393 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.084 (0.576)
95% CI		(1.320, 12.639)
Log-rank p-value		0.009

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.8, 100.0)	94.1 (91.7, 96.4)
6 months	96.0 (91.0, 100.0)	92.8 (89.9, 95.7)
9 months	96.0 (91.0, 100.0)	92.8 (89.9, 95.7)
12 months	96.0 (91.0, 100.0)	92.8 (89.9, 95.7)
18 months	NE (NE, NE)	92.8 (89.9, 95.7)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	4 (1.8)	14 (3.3)
Number of Subjects Censored, n (%)	213 (98.2)	405 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.485 (0.577)
95% CI		(0.480, 4.598)
Log-rank p-value		0.493

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (96.2, 99.9)	96.7 (95.0, 98.5)
6 months	98.1 (96.2, 99.9)	96.0 (93.8, 98.3)
9 months	98.1 (96.2, 99.9)	96.0 (93.8, 98.3)
12 months	98.1 (96.2, 99.9)	96.0 (93.8, 98.3)
18 months	NE (NE, NE)	96.0 (93.8, 98.3)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	2 (0.9)	11 (2.6)
Number of Subjects Censored, n (%)	215 (99.1)	408 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.093 (0.784)
95% CI		(0.450, 9.733)
Log-rank p-value		0.330

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.8, 100.0)	98.0 (96.7, 99.4)
6 months	99.1 (97.8, 100.0)	97.4 (95.5, 99.2)
9 months	99.1 (97.8, 100.0)	94.1 (89.3, 99.0)
12 months	99.1 (97.8, 100.0)	94.1 (89.3, 99.0)
18 months	NE (NE, NE)	94.1 (89.3, 99.0)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	0	10 (2.4)
Number of Subjects Censored, n (%)	217 (100.0)	409 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.019

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.4 (95.8, 99.0)
6 months	100.0 (100.0, 100.0)	97.4 (95.8, 99.0)
9 months	100.0 (100.0, 100.0)	97.4 (95.8, 99.0)
12 months	100.0 (100.0, 100.0)	97.4 (95.8, 99.0)
18 months	NE (NE, NE)	97.4 (95.8, 99.0)
Median Follow-up Time (months)	2.83	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	26 (12.0)	142 (33.9)
Number of Subjects Censored, n (%)	191 (88.0)	277 (66.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.58 (1.12, 2.04)
Median (95% CI)	NE (NE, NE)	13.14 (13.14, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.14, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.778 (0.214)
95% CI		(1.825, 4.229)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.1 (83.7, 92.5)	68.2 (63.6, 72.7)
6 months	85.5 (78.9, 92.1)	62.8 (57.5, 68.1)
9 months	85.5 (78.9, 92.1)	60.5 (54.4, 66.6)
12 months	85.5 (78.9, 92.1)	60.5 (54.4, 66.6)
18 months	NE (NE, NE)	40.3 (7.8, 72.9)
Median Follow-up Time (months)	2.79	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	6 (2.8)	82 (19.6)
Number of Subjects Censored, n (%)	211 (97.2)	337 (80.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.11, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.618 (0.424)
95% CI		(2.883, 15.194)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (94.9, 99.4)	82.3 (78.6, 86.0)
6 months	97.1 (94.9, 99.4)	77.5 (72.8, 82.2)
9 months	97.1 (94.9, 99.4)	76.2 (70.9, 81.5)
12 months	97.1 (94.9, 99.4)	76.2 (70.9, 81.5)
18 months	NE (NE, NE)	76.2 (70.9, 81.5)
Median Follow-up Time (months)	2.83	3.09

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	7 (3.2)	16 (3.8)
Number of Subjects Censored, n (%)	210 (96.8)	403 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.109 (0.454)
95% CI		(0.455, 2.703)
Log-rank p-value		0.824

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.7 (94.3, 99.1)	96.0 (94.1, 97.9)
6 months	96.7 (94.3, 99.1)	96.0 (94.1, 97.9)
9 months	96.7 (94.3, 99.1)	96.0 (94.1, 97.9)
12 months	96.7 (94.3, 99.1)	96.0 (94.1, 97.9)
18 months	NE (NE, NE)	96.0 (94.1, 97.9)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	3 (1.4)	12 (2.9)
Number of Subjects Censored, n (%)	214 (98.6)	407 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.764 (0.651)
95% CI		(0.493, 6.314)
Log-rank p-value		0.391

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.6, 100.0)	97.2 (95.6, 98.9)
6 months	96.5 (91.5, 100.0)	96.8 (95.0, 98.6)
9 months	96.5 (91.5, 100.0)	96.8 (95.0, 98.6)
12 months	96.5 (91.5, 100.0)	96.8 (95.0, 98.6)
18 months	NE (NE, NE)	96.8 (95.0, 98.6)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	36 (16.6)	105 (25.1)
Number of Subjects Censored, n (%)	181 (83.4)	314 (74.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.57 (2.56, 11.10)
Median (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.311 (0.195)
95% CI		(0.893, 1.923)
Log-rank p-value		0.179

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.0 (76.6, 87.4)	78.1 (74.0, 82.1)
6 months	82.0 (76.6, 87.4)	71.8 (66.7, 76.9)
9 months	82.0 (76.6, 87.4)	70.3 (64.8, 75.7)
12 months	82.0 (76.6, 87.4)	66.7 (58.3, 75.2)
18 months	NE (NE, NE)	66.7 (58.3, 75.2)
Median Follow-up Time (months)	2.69	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	11 (5.1)	39 (9.3)
Number of Subjects Censored, n (%)	206 (94.9)	380 (90.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
Median (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.613 (0.345)
95% CI		(0.820, 3.170)
Log-rank p-value		0.165

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (91.1, 97.6)	91.7 (89.1, 94.4)
6 months	94.4 (91.1, 97.6)	90.7 (87.7, 93.7)
9 months	94.4 (91.1, 97.6)	89.2 (85.5, 92.8)
12 months	94.4 (91.1, 97.6)	89.2 (85.5, 92.8)
18 months	NE (NE, NE)	89.2 (85.5, 92.8)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	7 (3.2)	7 (1.7)
Number of Subjects Censored, n (%)	210 (96.8)	412 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.4, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.477 (0.535)
95% CI		(0.167, 1.362)
Log-rank p-value		0.163

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.7 (94.3, 99.1)	98.2 (96.9, 99.5)
6 months	96.7 (94.3, 99.1)	98.2 (96.9, 99.5)
9 months	96.7 (94.3, 99.1)	98.2 (96.9, 99.5)
12 months	96.7 (94.3, 99.1)	98.2 (96.9, 99.5)
18 months	NE (NE, NE)	98.2 (96.9, 99.5)
Median Follow-up Time (months)	2.83	4.11

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	4 (1.8)	10 (2.4)
Number of Subjects Censored, n (%)	213 (98.2)	409 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.261 (0.592)
95% CI		(0.395, 4.023)
Log-rank p-value		0.715

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (96.1, 99.9)	97.6 (96.1, 99.1)
6 months	98.0 (96.1, 99.9)	97.6 (96.1, 99.1)
9 months	98.0 (96.1, 99.9)	97.6 (96.1, 99.1)
12 months	98.0 (96.1, 99.9)	97.6 (96.1, 99.1)
18 months	NE (NE, NE)	97.6 (96.1, 99.1)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	28 (12.9)	107 (25.5)
Number of Subjects Censored, n (%)	189 (87.1)	312 (74.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.91 (2.79, 6.47)
Median (95% CI)	NE (NE, NE)	13.60 (11.96, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.679 (0.218)
95% CI		(1.095, 2.573)
Log-rank p-value		0.022

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.3 (81.4, 91.2)	78.1 (74.0, 82.2)
6 months	83.7 (76.7, 90.6)	70.6 (65.3, 75.9)
9 months	83.7 (76.7, 90.6)	67.7 (61.8, 73.7)
12 months	83.7 (76.7, 90.6)	60.2 (45.3, 75.1)
18 months	NE (NE, NE)	40.1 (6.5, 73.8)
Median Follow-up Time (months)	2.79	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	12 (5.5)	75 (17.9)
Number of Subjects Censored, n (%)	205 (94.5)	344 (82.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.60 (5.78, NE)
Median (95% CI)	NE (NE, NE)	NE (13.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.2*, 13.0*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.908 (0.325)
95% CI		(1.538, 5.500)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.1 (90.8, 97.3)	84.2 (80.5, 87.8)
6 months	94.1 (90.8, 97.3)	79.4 (74.8, 83.9)
9 months	94.1 (90.8, 97.3)	76.5 (70.6, 82.5)
12 months	94.1 (90.8, 97.3)	76.5 (70.6, 82.5)
18 months	NE (NE, NE)	51.0 (10.0, 92.0)
Median Follow-up Time (months)	2.83	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	3 (1.4)	9 (2.1)
Number of Subjects Censored, n (%)	214 (98.6)	410 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.364 (0.671)
95% CI		(0.366, 5.079)
Log-rank p-value		0.657

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (97.0, 100.0)	98.0 (96.7, 99.4)
6 months	98.6 (97.0, 100.0)	97.6 (96.0, 99.2)
9 months	98.6 (97.0, 100.0)	97.6 (96.0, 99.2)
12 months	98.6 (97.0, 100.0)	97.6 (96.0, 99.2)
18 months	NE (NE, NE)	97.6 (96.0, 99.2)
Median Follow-up Time (months)	2.83	4.11

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	25 (11.5)	92 (22.0)
Number of Subjects Censored, n (%)	192 (88.5)	327 (78.0)
Time to first TEAE (months)		
25% percentile (95% CI)	5.78 (4.34, NE)	5.91 (3.81, 6.93)
Median (95% CI)	NE (5.78, NE)	NE (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.301 (0.232)
95% CI		(0.825, 2.051)
Log-rank p-value		0.214

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.4 (85.1, 93.7)	83.4 (79.7, 87.1)
6 months	71.0 (50.4, 91.6)	74.4 (69.0, 79.7)
9 months	71.0 (50.4, 91.6)	64.6 (56.9, 72.3)
12 months	71.0 (50.4, 91.6)	60.0 (48.7, 71.3)
18 months	NE (NE, NE)	60.0 (48.7, 71.3)
Median Follow-up Time (months)	2.83	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	7 (3.2)	18 (4.3)
Number of Subjects Censored, n (%)	210 (96.8)	401 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.2, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.903 (0.462)
95% CI		(0.365, 2.235)
Log-rank p-value		0.896

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (96.3, 99.9)	96.8 (95.0, 98.5)
6 months	90.4 (81.3, 99.4)	95.6 (93.2, 98.0)
9 months	90.4 (81.3, 99.4)	93.0 (89.2, 96.7)
12 months	90.4 (81.3, 99.4)	93.0 (89.2, 96.7)
18 months	NE (NE, NE)	93.0 (89.2, 96.7)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	5 (2.3)	12 (2.9)
Number of Subjects Censored, n (%)	212 (97.7)	407 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.56, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.612 (0.561)
95% CI		(0.204, 1.838)
Log-rank p-value		0.369

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.9 (95.8, 100.0)	98.7 (97.5, 99.8)
6 months	94.3 (87.0, 100.0)	96.2 (93.7, 98.6)
9 months	94.3 (87.0, 100.0)	95.3 (92.3, 98.3)
12 months	94.3 (87.0, 100.0)	90.3 (80.3, 100.0)
18 months	NE (NE, NE)	90.3 (80.3, 100.0)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	1 (0.5)	11 (2.6)
Number of Subjects Censored, n (%)	216 (99.5)	408 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.910 (1.054)
95% CI		(0.496, 30.849)
Log-rank p-value		0.158

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.6, 100.0)	97.3 (95.6, 99.0)
6 months	99.5 (98.6, 100.0)	96.6 (94.5, 98.7)
9 months	99.5 (98.6, 100.0)	96.6 (94.5, 98.7)
12 months	99.5 (98.6, 100.0)	96.6 (94.5, 98.7)
18 months	NE (NE, NE)	96.6 (94.5, 98.7)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	35 (16.1)	64 (15.3)
Number of Subjects Censored, n (%)	182 (83.9)	355 (84.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.77, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.812 (0.219)
95% CI		(0.529, 1.247)
Log-rank p-value		0.371

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.1 (76.6, 87.5)	86.6 (83.2, 90.0)
6 months	82.1 (76.6, 87.5)	82.4 (78.0, 86.8)
9 months	82.1 (76.6, 87.5)	79.8 (74.7, 84.9)
12 months	82.1 (76.6, 87.5)	79.8 (74.7, 84.9)
18 months	NE (NE, NE)	79.8 (74.7, 84.9)
Median Follow-up Time (months)	2.79	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	27 (12.4)	34 (8.1)
Number of Subjects Censored, n (%)	190 (87.6)	385 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	17.74 (17.74, NE)
Median (95% CI)	NE (NE, NE)	17.74 (17.74, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.74, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.490 (0.275)
95% CI		(0.286, 0.841)
Log-rank p-value		0.010

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.7 (80.6, 90.8)	94.1 (91.7, 96.4)
6 months	85.7 (80.6, 90.8)	89.8 (86.0, 93.5)
9 months	85.7 (80.6, 90.8)	88.3 (84.0, 92.5)
12 months	85.7 (80.6, 90.8)	88.3 (84.0, 92.5)
18 months	NE (NE, NE)	44.1 (0.0, 100.0)
Median Follow-up Time (months)	2.79	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	2 (0.9)	29 (6.9)
Number of Subjects Censored, n (%)	215 (99.1)	390 (93.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		7.209 (0.731)
95% CI		(1.719, 30.232)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.6, 100.0)	92.8 (90.2, 95.3)
6 months	99.0 (97.6, 100.0)	92.8 (90.2, 95.3)
9 months	99.0 (97.6, 100.0)	92.8 (90.2, 95.3)
12 months	99.0 (97.6, 100.0)	92.8 (90.2, 95.3)
18 months	NE (NE, NE)	92.8 (90.2, 95.3)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Endocrine disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	1 (0.5)	94 (22.4)
Number of Subjects Censored, n (%)	216 (99.5)	325 (77.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.52 (3.81, 6.47)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		38.458 (1.006)
95% CI		(5.352, 276.366)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Endocrine disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.6, 100.0)	81.6 (77.7, 85.4)
6 months	99.5 (98.6, 100.0)	71.0 (65.2, 76.8)
9 months	99.5 (98.6, 100.0)	68.2 (61.8, 74.6)
12 months	99.5 (98.6, 100.0)	65.6 (57.6, 73.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	1 (0.5)	88 (21.0)
Number of Subjects Censored, n (%)	216 (99.5)	331 (79.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.75 (4.17, 9.33)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		35.072 (1.007)
95% CI		(4.875, 252.308)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.6, 100.0)	83.1 (79.4, 86.8)
6 months	99.5 (98.6, 100.0)	73.2 (67.5, 78.8)
9 months	99.5 (98.6, 100.0)	69.1 (62.4, 75.7)
12 months	99.5 (98.6, 100.0)	66.5 (58.4, 74.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	16 (7.4)	53 (12.6)
Number of Subjects Censored, n (%)	201 (92.6)	366 (87.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.331 (0.298)
95% CI		(0.742, 2.386)
Log-rank p-value		0.323

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.6 (88.9, 96.2)	89.1 (85.9, 92.2)
6 months	90.9 (86.0, 95.7)	84.1 (79.8, 88.4)
9 months	90.9 (86.0, 95.7)	83.2 (78.6, 87.8)
12 months	90.9 (86.0, 95.7)	83.2 (78.6, 87.8)
18 months	NE (NE, NE)	83.2 (78.6, 87.8)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	11 (5.1)	24 (5.7)
Number of Subjects Censored, n (%)	206 (94.9)	395 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.824 (0.389)
95% CI		(0.384, 1.764)
Log-rank p-value		0.637

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.6 (91.5, 97.7)	94.8 (92.5, 97.1)
6 months	94.6 (91.5, 97.7)	92.9 (90.0, 95.8)
9 months	94.6 (91.5, 97.7)	92.0 (88.6, 95.4)
12 months	94.6 (91.5, 97.7)	92.0 (88.6, 95.4)
18 months	NE (NE, NE)	92.0 (88.6, 95.4)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	2 (0.9)	10 (2.4)
Number of Subjects Censored, n (%)	215 (99.1)	409 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.768 (0.790)
95% CI		(0.376, 8.317)
Log-rank p-value		0.467

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.4, 100.0)	97.5 (95.9, 99.1)
6 months	97.7 (94.2, 100.0)	96.9 (94.9, 98.9)
9 months	97.7 (94.2, 100.0)	96.9 (94.9, 98.9)
12 months	97.7 (94.2, 100.0)	96.9 (94.9, 98.9)
18 months	NE (NE, NE)	96.9 (94.9, 98.9)
Median Follow-up Time (months)	2.83	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	2 (0.9)	10 (2.4)
Number of Subjects Censored, n (%)	215 (99.1)	409 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.040 (0.782)
95% CI		(0.440, 9.453)
Log-rank p-value		0.347

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (97.4, 100.0)	98.0 (96.5, 99.4)
6 months	98.9 (97.4, 100.0)	96.9 (94.9, 98.9)
9 months	98.9 (97.4, 100.0)	96.9 (94.9, 98.9)
12 months	98.9 (97.4, 100.0)	96.9 (94.9, 98.9)
18 months	NE (NE, NE)	96.9 (94.9, 98.9)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	24 (11.1)	48 (11.5)
Number of Subjects Censored, n (%)	193 (88.9)	371 (88.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.789 (0.254)
95% CI		(0.479, 1.299)
Log-rank p-value		0.358

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (84.7, 93.2)	89.4 (86.3, 92.5)
6 months	87.3 (82.1, 92.6)	86.2 (82.3, 90.1)
9 months	87.3 (82.1, 92.6)	86.2 (82.3, 90.1)
12 months	87.3 (82.1, 92.6)	83.7 (77.6, 89.8)
18 months	NE (NE, NE)	83.7 (77.6, 89.8)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	3 (1.4)	19 (4.5)
Number of Subjects Censored, n (%)	214 (98.6)	400 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.366 (0.627)
95% CI		(0.692, 8.086)
Log-rank p-value		0.170

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.7, 100.0)	95.7 (93.6, 97.8)
6 months	98.4 (96.7, 100.0)	94.6 (92.0, 97.1)
9 months	98.4 (96.7, 100.0)	94.6 (92.0, 97.1)
12 months	98.4 (96.7, 100.0)	91.9 (86.1, 97.6)
18 months	NE (NE, NE)	91.9 (86.1, 97.6)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3F
Summary of Time to Onset of TEAE by SOC/PT by Duration of Metastatic Disease
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
> 18 months

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Number of Subjects with Events, n (%)	2 (0.9)	13 (3.1)
Number of Subjects Censored, n (%)	215 (99.1)	406 (96.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.490 (0.768)
95% CI		(0.553, 11.209)
Log-rank p-value		0.200

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Colon

Statistics	Placebo + BSC N=217	Fruquintinib + BSC N=419
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.8, 100.0)	97.2 (95.6, 98.8)
6 months	99.1 (97.8, 100.0)	96.1 (93.9, 98.4)
9 months	99.1 (97.8, 100.0)	96.1 (93.9, 98.4)
12 months	99.1 (97.8, 100.0)	96.1 (93.9, 98.4)
18 months	NE (NE, NE)	96.1 (93.9, 98.4)
Median Follow-up Time (months)	2.83	4.17

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	88 (63.8)	186 (67.4)
Number of Subjects Censored, n (%)	50 (36.2)	90 (32.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.56 (0.23, 0.69)	0.51 (0.30, 0.69)
Median (95% CI)	1.38 (0.95, 1.87)	1.41 (0.99, 1.87)
75% percentile (95% CI)	NE (3.19, NE)	6.93 (4.60, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Min, Max	0.0, 6.5*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.942 (0.132)
95% CI		(0.726, 1.221)
Log-rank p-value		0.568

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	34.9 (26.6, 43.2)	40.0 (34.1, 45.9)
6 months	32.0 (22.6, 41.3)	26.2 (19.8, 32.6)
9 months	NE (NE, NE)	21.0 (13.7, 28.4)
12 months	NE (NE, NE)	21.0 (13.7, 28.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.36	1.41

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	33 (23.9)	84 (30.4)
Number of Subjects Censored, n (%)	105 (76.1)	192 (69.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.72, NE)	1.61 (0.95, 3.12)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.174 (0.208)
95% CI		(0.781, 1.766)
Log-rank p-value		0.456

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.4 (68.0, 82.7)	70.8 (65.3, 76.3)
6 months	75.4 (68.0, 82.7)	66.7 (60.6, 72.9)
9 months	NE (NE, NE)	66.7 (60.6, 72.9)
12 months	NE (NE, NE)	66.7 (60.6, 72.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.28	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	25 (18.1)	59 (21.4)
Number of Subjects Censored, n (%)	113 (81.9)	217 (78.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.64, NE)	7.29 (2.83, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.092 (0.243)
95% CI		(0.678, 1.758)
Log-rank p-value		0.721

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.3 (74.6, 87.9)	80.1 (75.3, 85.0)
6 months	81.3 (74.6, 87.9)	76.7 (71.3, 82.2)
9 months	NE (NE, NE)	74.8 (68.2, 81.3)
12 months	NE (NE, NE)	74.8 (68.2, 81.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.46	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	14 (10.1)	30 (10.9)
Number of Subjects Censored, n (%)	124 (89.9)	246 (89.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.5*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.942 (0.332)
95% CI		(0.492, 1.806)
Log-rank p-value		0.754

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.0 (82.0, 94.1)	90.5 (87.0, 94.1)
6 months	88.0 (82.0, 94.1)	88.6 (84.5, 92.7)
9 months	NE (NE, NE)	85.9 (80.5, 91.3)
12 months	NE (NE, NE)	85.9 (80.5, 91.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.74	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	6 (4.3)	40 (14.5)
Number of Subjects Censored, n (%)	132 (95.7)	236 (85.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.26, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.1, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.994 (0.442)
95% CI		(1.259, 7.121)
Log-rank p-value		0.009

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.3 (91.7, 99.0)	87.5 (83.5, 91.4)
6 months	95.3 (91.7, 99.0)	84.6 (79.9, 89.3)
9 months	NE (NE, NE)	80.5 (73.2, 87.7)
12 months	NE (NE, NE)	80.5 (73.2, 87.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.78	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	20 (14.5)	17 (6.2)
Number of Subjects Censored, n (%)	118 (85.5)	259 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.19, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.8*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.255 (0.351)
95% CI		(0.128, 0.507)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.9 (78.4, 91.5)	96.1 (93.7, 98.5)
6 months	77.3 (65.3, 89.2)	91.8 (87.7, 95.9)
9 months	NE (NE, NE)	91.8 (87.7, 95.9)
12 months	NE (NE, NE)	91.8 (87.7, 95.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	12 (8.7)	15 (5.4)
Number of Subjects Censored, n (%)	126 (91.3)	261 (94.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.614 (0.390)
95% CI		(0.286, 1.319)
Log-rank p-value		0.208

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.6 (85.4, 95.8)	94.4 (91.6, 97.1)
6 months	90.6 (85.4, 95.8)	94.4 (91.6, 97.1)
9 months	NE (NE, NE)	94.4 (91.6, 97.1)
12 months	NE (NE, NE)	94.4 (91.6, 97.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	5 (3.6)	10 (3.6)
Number of Subjects Censored, n (%)	133 (96.4)	266 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.7, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.566 (0.585)
95% CI		(0.180, 1.781)
Log-rank p-value		0.275

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.1 (92.7, 99.5)	98.1 (96.4, 99.8)
6 months	96.1 (92.7, 99.5)	95.1 (91.8, 98.5)
9 months	NE (NE, NE)	92.7 (87.1, 98.4)
12 months	NE (NE, NE)	92.7 (87.1, 98.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	1 (0.7)	7 (2.5)
Number of Subjects Censored, n (%)	137 (99.3)	269 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.4, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.358 (1.097)
95% CI		(0.274, 20.259)
Log-rank p-value		0.439

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	98.0 (96.2, 99.7)
6 months	99.3 (97.8, 100.0)	97.2 (94.8, 99.5)
9 months	NE (NE, NE)	94.8 (89.6, 99.9)
12 months	NE (NE, NE)	94.8 (89.6, 99.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	1 (0.7)	7 (2.5)
Number of Subjects Censored, n (%)	137 (99.3)	269 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.146 (1.085)
95% CI		(0.375, 26.388)
Log-rank p-value		0.244

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	98.2 (96.6, 99.8)
6 months	99.3 (97.8, 100.0)	96.1 (92.8, 99.5)
9 months	NE (NE, NE)	96.1 (92.8, 99.5)
12 months	NE (NE, NE)	96.1 (92.8, 99.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	76 (55.1)	197 (71.4)
Number of Subjects Censored, n (%)	62 (44.9)	79 (28.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.46 (0.30, 0.69)	0.48 (0.36, 0.69)
Median (95% CI)	1.71 (0.95, 3.75)	1.28 (0.85, 1.64)
75% percentile (95% CI)	5.36 (3.75, NE)	4.70 (3.58, 7.75)
Min, Max	0.0, 5.6*	0.0, 10.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.201 (0.138)
95% CI		(0.916, 1.573)
Log-rank p-value		0.120

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	41.4 (31.4, 51.3)	34.8 (29.0, 40.7)
6 months	NE (NE, NE)	19.5 (13.1, 25.9)
9 months	NE (NE, NE)	16.3 (9.5, 23.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.23	1.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	16 (11.6)	72 (26.1)
Number of Subjects Censored, n (%)	122 (88.4)	204 (73.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.71 (1.87, 7.33)
Median (95% CI)	NE (NE, NE)	NE (10.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.111 (0.279)
95% CI		(1.221, 3.649)
Log-rank p-value		0.006

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.2 (82.8, 93.7)	76.8 (71.7, 81.9)
6 months	88.2 (82.8, 93.7)	69.2 (62.3, 76.2)
9 months	NE (NE, NE)	67.1 (59.3, 75.0)
12 months	NE (NE, NE)	56.0 (34.9, 77.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.58	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	27 (19.6)	47 (17.0)
Number of Subjects Censored, n (%)	111 (80.4)	229 (83.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.35, NE)	9.20 (5.68, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.689 (0.250)
95% CI		(0.423, 1.124)
Log-rank p-value		0.139

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.7 (72.7, 86.6)	85.0 (80.6, 89.4)
6 months	79.7 (72.7, 86.6)	80.5 (74.7, 86.3)
9 months	NE (NE, NE)	76.5 (68.6, 84.4)
12 months	NE (NE, NE)	72.5 (61.8, 83.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.51	3.33

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	21 (15.2)	55 (19.9)
Number of Subjects Censored, n (%)	117 (84.8)	221 (80.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.92, NE)	7.75 (3.71, NE)
Median (95% CI)	NE (NE, NE)	NE (10.12, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.968 (0.267)
95% CI		(0.573, 1.634)
Log-rank p-value		0.901

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.6 (73.3, 89.9)	83.3 (78.7, 87.9)
6 months	81.6 (73.3, 89.9)	79.1 (73.5, 84.6)
9 months	NE (NE, NE)	72.0 (63.6, 80.5)
12 months	NE (NE, NE)	62.2 (47.1, 77.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	14 (10.1)	59 (21.4)
Number of Subjects Censored, n (%)	124 (89.9)	217 (78.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.62 (3.19, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.846 (0.302)
95% CI		(1.021, 3.338)
Log-rank p-value		0.038

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.0 (79.0, 95.0)	81.1 (76.3, 85.9)
6 months	87.0 (79.0, 95.0)	74.1 (67.8, 80.5)
9 months	NE (NE, NE)	72.4 (65.3, 79.4)
12 months	NE (NE, NE)	72.4 (65.3, 79.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	17 (12.3)	38 (13.8)
Number of Subjects Censored, n (%)	121 (87.7)	238 (86.2)
Time to first TEAE (months)		
25% percentile (95% CI)	5.36 (5.36, NE)	10.18 (7.39, NE)
Median (95% CI)	NE (5.36, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.823 (0.305)
95% CI		(0.453, 1.496)
Log-rank p-value		0.522

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.3 (81.5, 93.2)	88.8 (84.9, 92.7)
6 months	74.9 (51.7, 98.1)	84.1 (78.8, 89.4)
9 months	NE (NE, NE)	82.0 (75.4, 88.5)
12 months	NE (NE, NE)	71.5 (56.4, 86.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	4 (2.9)	44 (15.9)
Number of Subjects Censored, n (%)	134 (97.1)	232 (84.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.98, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.611 (0.526)
95% CI		(2.003, 15.721)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (94.0, 99.9)	85.5 (81.3, 89.7)
6 months	96.9 (94.0, 99.9)	82.2 (77.0, 87.4)
9 months	NE (NE, NE)	80.0 (73.3, 86.6)
12 months	NE (NE, NE)	80.0 (73.3, 86.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	6 (4.3)	21 (7.6)
Number of Subjects Censored, n (%)	132 (95.7)	255 (92.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.395 (0.473)
95% CI		(0.552, 3.525)
Log-rank p-value		0.468

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (91.9, 99.0)	93.9 (90.9, 96.8)
6 months	95.5 (91.9, 99.0)	90.2 (86.0, 94.4)
9 months	NE (NE, NE)	90.2 (86.0, 94.4)
12 months	NE (NE, NE)	90.2 (86.0, 94.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	1 (0.7)	6 (2.2)
Number of Subjects Censored, n (%)	137 (99.3)	270 (97.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.725 (1.081)
95% CI		(0.447, 31.020)
Log-rank p-value		0.191

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	97.8 (96.1, 99.5)
6 months	99.3 (97.9, 100.0)	97.8 (96.1, 99.5)
9 months	NE (NE, NE)	97.8 (96.1, 99.5)
12 months	NE (NE, NE)	97.8 (96.1, 99.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	3 (2.2)	9 (3.3)
Number of Subjects Censored, n (%)	135 (97.8)	267 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.141 (0.677)
95% CI		(0.303, 4.304)
Log-rank p-value		0.857

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (94.5, 100.0)	96.5 (94.2, 98.8)
6 months	97.4 (94.5, 100.0)	96.5 (94.2, 98.8)
9 months	NE (NE, NE)	96.5 (94.2, 98.8)
12 months	NE (NE, NE)	96.5 (94.2, 98.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	9 (6.5)	3 (1.1)
Number of Subjects Censored, n (%)	129 (93.5)	273 (98.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 6.8*	0.8*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.122 (0.691)
95% CI		(0.031, 0.472)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.0 (88.6, 97.4)	99.2 (98.1, 100.0)
6 months	93.0 (88.6, 97.4)	97.9 (95.1, 100.0)
9 months	NE (NE, NE)	97.9 (95.1, 100.0)
12 months	NE (NE, NE)	97.9 (95.1, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	0	8 (2.9)
Number of Subjects Censored, n (%)	138 (100.0)	268 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.3, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.063

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.3 (95.2, 99.3)
6 months	100.0 (100.0, 100.0)	97.3 (95.2, 99.3)
9 months	NE (NE, NE)	94.6 (89.2, 100.0)
12 months	NE (NE, NE)	94.6 (89.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	44 (31.9)	115 (41.7)
Number of Subjects Censored, n (%)	94 (68.1)	161 (58.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.69, 2.83)	1.08 (0.82, 1.64)
Median (95% CI)	NE (NE, NE)	9.43 (4.63, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.148 (0.181)
95% CI		(0.805, 1.636)
Log-rank p-value		0.516

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	66.8 (58.7, 75.0)	60.7 (54.7, 66.7)
6 months	66.8 (58.7, 75.0)	56.6 (50.2, 63.1)
9 months	NE (NE, NE)	51.1 (43.2, 58.9)
12 months	NE (NE, NE)	47.2 (36.8, 57.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.22	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	29 (21.0)	77 (27.9)
Number of Subjects Censored, n (%)	109 (79.0)	199 (72.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.68, NE)	2.92 (1.61, 5.36)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.185 (0.222)
95% CI		(0.766, 1.833)
Log-rank p-value		0.513

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.8 (70.6, 85.0)	73.4 (68.0, 78.9)
6 months	77.8 (70.6, 85.0)	68.9 (62.7, 75.2)
9 months	NE (NE, NE)	67.6 (61.0, 74.3)
12 months	NE (NE, NE)	63.7 (53.8, 73.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.50	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	3 (2.2)	16 (5.8)
Number of Subjects Censored, n (%)	135 (97.8)	260 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.7, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.139 (0.640)
95% CI		(0.611, 7.492)
Log-rank p-value		0.215

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.4, 100.0)	94.5 (91.6, 97.3)
6 months	97.8 (95.4, 100.0)	93.7 (90.6, 96.9)
9 months	NE (NE, NE)	91.4 (85.9, 96.9)
12 months	NE (NE, NE)	91.4 (85.9, 96.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	3 (2.2)	13 (4.7)
Number of Subjects Censored, n (%)	135 (97.8)	263 (95.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 6.8*	0.6, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.524 (0.656)
95% CI		(0.422, 5.507)
Log-rank p-value		0.548

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.3, 100.0)	96.1 (93.7, 98.5)
6 months	97.8 (95.3, 100.0)	93.9 (90.1, 97.8)
9 months	NE (NE, NE)	91.8 (86.1, 97.4)
12 months	NE (NE, NE)	91.8 (86.1, 97.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	2 (1.4)	8 (2.9)
Number of Subjects Censored, n (%)	136 (98.6)	268 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.7, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.638 (0.809)
95% CI		(0.335, 8.003)
Log-rank p-value		0.627

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.5, 100.0)	97.2 (95.2, 99.3)
6 months	98.5 (96.5, 100.0)	96.6 (94.2, 99.0)
9 months	NE (NE, NE)	96.6 (94.2, 99.0)
12 months	NE (NE, NE)	96.6 (94.2, 99.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	2 (1.4)	10 (3.6)
Number of Subjects Censored, n (%)	136 (98.6)	266 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.3, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.193 (0.787)
95% CI		(0.469, 10.254)
Log-rank p-value		0.310

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.5, 100.0)	96.5 (94.2, 98.7)
6 months	98.5 (96.5, 100.0)	96.5 (94.2, 98.7)
9 months	NE (NE, NE)	94.2 (89.4, 99.1)
12 months	NE (NE, NE)	94.2 (89.4, 99.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	0	13 (4.7)
Number of Subjects Censored, n (%)	138 (100.0)	263 (95.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.7, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.015

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.9 (93.5, 98.3)
6 months	100.0 (100.0, 100.0)	94.3 (91.2, 97.5)
9 months	NE (NE, NE)	94.3 (91.2, 97.5)
12 months	NE (NE, NE)	94.3 (91.2, 97.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	2 (1.4)	9 (3.3)
Number of Subjects Censored, n (%)	136 (98.6)	267 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.932 (0.796)
95% CI		(0.406, 9.198)
Log-rank p-value		0.421

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (94.7, 100.0)	96.9 (94.8, 99.0)
6 months	97.8 (94.7, 100.0)	96.9 (94.8, 99.0)
9 months	NE (NE, NE)	95.5 (92.0, 99.0)
12 months	NE (NE, NE)	95.5 (92.0, 99.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	1 (0.7)	5 (1.8)
Number of Subjects Censored, n (%)	137 (99.3)	271 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.8*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.880 (1.114)
95% CI		(0.212, 16.669)
Log-rank p-value		0.607

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	98.4 (96.8, 100.0)
6 months	99.3 (97.8, 100.0)	97.2 (94.4, 100.0)
9 months	NE (NE, NE)	97.2 (94.4, 100.0)
12 months	NE (NE, NE)	97.2 (94.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	1 (0.7)	7 (2.5)
Number of Subjects Censored, n (%)	137 (99.3)	269 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.7, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.097 (1.078)
95% CI		(0.374, 25.639)
Log-rank p-value		0.273

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	97.2 (95.2, 99.3)
6 months	99.3 (97.8, 100.0)	97.2 (95.2, 99.3)
9 months	NE (NE, NE)	97.2 (95.2, 99.3)
12 months	NE (NE, NE)	97.2 (95.2, 99.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	1 (0.7)	8 (2.9)
Number of Subjects Censored, n (%)	137 (99.3)	268 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.7, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.599 (1.097)
95% CI		(0.303, 22.311)
Log-rank p-value		0.439

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.6, 100.0)	98.3 (96.5, 100.0)
6 months	99.2 (97.6, 100.0)	94.8 (91.1, 98.6)
9 months	NE (NE, NE)	94.8 (91.1, 98.6)
12 months	NE (NE, NE)	94.8 (91.1, 98.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	38 (27.5)	113 (40.9)
Number of Subjects Censored, n (%)	100 (72.5)	163 (59.1)
Time to first TEAE (months)		
25% percentile (95% CI)	1.94 (0.95, NE)	1.58 (0.95, 1.68)
Median (95% CI)	NE (5.82, NE)	6.90 (5.78, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.349 (0.191)
95% CI		(0.928, 1.961)
Log-rank p-value		0.110

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.3 (63.4, 79.3)	62.2 (56.3, 68.1)
6 months	57.1 (31.3, 82.9)	56.9 (50.0, 63.7)
9 months	NE (NE, NE)	46.5 (37.4, 55.6)
12 months	NE (NE, NE)	46.5 (37.4, 55.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.66	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	12 (8.7)	36 (13.0)
Number of Subjects Censored, n (%)	126 (91.3)	240 (87.0)
Time to first TEAE (months)		
25% percentile (95% CI)	5.82 (5.82, NE)	NE (7.85, NE)
Median (95% CI)	NE (5.82, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.5*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.162 (0.344)
95% CI		(0.592, 2.282)
Log-rank p-value		0.661

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (84.2, 95.8)	88.9 (85.1, 92.7)
6 months	72.0 (40.1, 100.0)	84.7 (79.5, 89.9)
9 months	NE (NE, NE)	80.6 (73.0, 88.1)
12 months	NE (NE, NE)	80.6 (73.0, 88.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	8 (5.8)	30 (10.9)
Number of Subjects Censored, n (%)	130 (94.2)	246 (89.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.43, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.349 (0.409)
95% CI		(0.605, 3.008)
Log-rank p-value		0.456

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.0 (90.0, 98.0)	90.9 (87.5, 94.4)
6 months	94.0 (90.0, 98.0)	87.9 (83.0, 92.8)
9 months	NE (NE, NE)	82.9 (75.6, 90.1)
12 months	NE (NE, NE)	82.9 (75.6, 90.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	6 (4.3)	29 (10.5)
Number of Subjects Censored, n (%)	132 (95.7)	247 (89.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.7, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.852 (0.456)
95% CI		(0.757, 4.531)
Log-rank p-value		0.182

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (92.1, 99.0)	90.9 (87.5, 94.4)
6 months	95.6 (92.1, 99.0)	89.5 (85.5, 93.4)
9 months	NE (NE, NE)	84.4 (77.6, 91.2)
12 months	NE (NE, NE)	84.4 (77.6, 91.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	7 (5.1)	24 (8.7)
Number of Subjects Censored, n (%)	131 (94.9)	252 (91.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.4, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.289 (0.441)
95% CI		(0.543, 3.058)
Log-rank p-value		0.643

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (91.2, 98.6)	93.0 (89.9, 96.2)
6 months	94.9 (91.2, 98.6)	89.8 (85.4, 94.1)
9 months	NE (NE, NE)	86.1 (79.6, 92.6)
12 months	NE (NE, NE)	86.1 (79.6, 92.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	1 (0.7)	18 (6.5)
Number of Subjects Censored, n (%)	137 (99.3)	258 (93.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.7, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.514 (1.034)
95% CI		(0.858, 49.456)
Log-rank p-value		0.037

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.0, 100.0)	94.6 (91.8, 97.3)
6 months	99.0 (97.0, 100.0)	93.6 (90.2, 96.9)
9 months	NE (NE, NE)	87.3 (79.0, 95.5)
12 months	NE (NE, NE)	87.3 (79.0, 95.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	5 (3.6)	16 (5.8)
Number of Subjects Censored, n (%)	133 (96.4)	260 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.5, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.081 (0.525)
95% CI		(0.386, 3.025)
Log-rank p-value		0.850

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.2 (92.9, 99.5)	95.1 (92.5, 97.7)
6 months	96.2 (92.9, 99.5)	93.1 (89.3, 96.9)
9 months	NE (NE, NE)	91.7 (87.0, 96.4)
12 months	NE (NE, NE)	91.7 (87.0, 96.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	1 (0.7)	18 (6.5)
Number of Subjects Censored, n (%)	137 (99.3)	258 (93.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.5, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		7.040 (1.033)
95% CI		(0.930, 53.298)
Log-rank p-value		0.027

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	93.7 (90.7, 96.7)
6 months	99.3 (97.9, 100.0)	92.1 (88.4, 95.8)
9 months	NE (NE, NE)	92.1 (88.4, 95.8)
12 months	NE (NE, NE)	92.1 (88.4, 95.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	2 (1.4)	11 (4.0)
Number of Subjects Censored, n (%)	136 (98.6)	265 (96.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.7, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.439 (0.778)
95% CI		(0.531, 11.204)
Log-rank p-value		0.219

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (95.9, 100.0)	95.9 (93.4, 98.4)
6 months	98.3 (95.9, 100.0)	95.9 (93.4, 98.4)
9 months	NE (NE, NE)	94.6 (90.9, 98.2)
12 months	NE (NE, NE)	94.6 (90.9, 98.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	0	11 (4.0)
Number of Subjects Censored, n (%)	138 (100.0)	265 (96.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.8*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.041

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.4 (94.1, 98.7)
6 months	100.0 (100.0, 100.0)	95.6 (92.7, 98.4)
9 months	NE (NE, NE)	93.6 (89.0, 98.3)
12 months	NE (NE, NE)	93.6 (89.0, 98.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	1 (0.7)	9 (3.3)
Number of Subjects Censored, n (%)	137 (99.3)	267 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.8*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.519 (1.063)
95% CI		(0.438, 28.271)
Log-rank p-value		0.200

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	96.9 (94.8, 99.0)
6 months	99.3 (97.8, 100.0)	96.9 (94.8, 99.0)
9 months	NE (NE, NE)	95.0 (90.8, 99.2)
12 months	NE (NE, NE)	95.0 (90.8, 99.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	35 (25.4)	106 (38.4)
Number of Subjects Censored, n (%)	103 (74.6)	170 (61.6)
Time to first TEAE (months)		
25% percentile (95% CI)	1.84 (0.95, NE)	0.87 (0.69, 1.54)
Median (95% CI)	NE (NE, NE)	9.69 (9.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.547 (0.198)
95% CI		(1.049, 2.281)
Log-rank p-value		0.035

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.4 (65.8, 81.1)	64.6 (58.9, 70.3)
6 months	73.4 (65.8, 81.1)	60.5 (54.2, 66.7)
9 months	NE (NE, NE)	57.6 (50.5, 64.7)
12 months	NE (NE, NE)	48.7 (35.7, 61.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.25	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	7 (5.1)	46 (16.7)
Number of Subjects Censored, n (%)	131 (94.9)	230 (83.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.616 (0.410)
95% CI		(1.620, 8.071)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.3 (90.2, 98.5)	83.4 (79.0, 87.8)
6 months	94.3 (90.2, 98.5)	82.8 (78.2, 87.3)
9 months	NE (NE, NE)	82.8 (78.2, 87.3)
12 months	NE (NE, NE)	82.8 (78.2, 87.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.19

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	14 (10.1)	26 (9.4)
Number of Subjects Censored, n (%)	124 (89.9)	250 (90.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.784 (0.340)
95% CI		(0.402, 1.526)
Log-rank p-value		0.451

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.7 (84.6, 94.8)	92.0 (88.6, 95.3)
6 months	89.7 (84.6, 94.8)	89.1 (84.8, 93.4)
9 months	NE (NE, NE)	87.7 (82.7, 92.7)
12 months	NE (NE, NE)	87.7 (82.7, 92.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	11 (8.0)	22 (8.0)
Number of Subjects Censored, n (%)	127 (92.0)	254 (92.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.909 (0.375)
95% CI		(0.436, 1.897)
Log-rank p-value		0.789

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.7 (87.0, 96.4)	92.1 (88.8, 95.4)
6 months	91.7 (87.0, 96.4)	91.4 (88.0, 94.9)
9 months	NE (NE, NE)	91.4 (88.0, 94.9)
12 months	NE (NE, NE)	91.4 (88.0, 94.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	2 (1.4)	10 (3.6)
Number of Subjects Censored, n (%)	136 (98.6)	266 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.327 (0.782)
95% CI		(0.502, 10.781)
Log-rank p-value		0.290

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.5, 100.0)	96.2 (93.8, 98.5)
6 months	98.5 (96.5, 100.0)	96.2 (93.8, 98.5)
9 months	NE (NE, NE)	96.2 (93.8, 98.5)
12 months	NE (NE, NE)	96.2 (93.8, 98.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	1 (0.7)	5 (1.8)
Number of Subjects Censored, n (%)	137 (99.3)	271 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.5, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.820 (1.119)
95% CI		(0.203, 16.321)
Log-rank p-value		0.629

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.4, 100.0)	98.5 (97.1, 100.0)
6 months	99.1 (97.4, 100.0)	98.5 (97.1, 100.0)
9 months	NE (NE, NE)	97.1 (94.0, 100.0)
12 months	NE (NE, NE)	97.1 (94.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Vascular disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	21 (15.2)	100 (36.2)
Number of Subjects Censored, n (%)	117 (84.8)	176 (63.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.61, NE)	1.18 (0.72, 1.94)
Median (95% CI)	NE (NE, NE)	NE (7.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.483 (0.243)
95% CI		(1.543, 3.995)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Vascular disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.1 (79.1, 91.1)	64.8 (59.0, 70.7)
6 months	79.0 (66.3, 91.8)	60.5 (53.9, 67.2)
9 months	NE (NE, NE)	57.0 (49.1, 64.9)
12 months	NE (NE, NE)	57.0 (49.1, 64.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.66	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	11 (8.0)	91 (33.0)
Number of Subjects Censored, n (%)	127 (92.0)	185 (67.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.61 (0.95, 2.63)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.401 (0.321)
95% CI		(2.345, 8.260)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.8 (87.1, 96.4)	67.9 (62.2, 73.6)
6 months	91.8 (87.1, 96.4)	65.8 (59.7, 71.8)
9 months	NE (NE, NE)	60.3 (52.2, 68.4)
12 months	NE (NE, NE)	60.3 (52.2, 68.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.78	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	29 (21.0)	86 (31.2)
Number of Subjects Censored, n (%)	109 (79.0)	190 (68.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.15, NE)	1.84 (0.99, 4.04)
Median (95% CI)	NE (NE, NE)	NE (9.76, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.435 (0.219)
95% CI		(0.935, 2.204)
Log-rank p-value		0.087

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.8 (70.5, 85.0)	70.1 (64.5, 75.6)
6 months	77.8 (70.5, 85.0)	67.2 (61.0, 73.4)
9 months	NE (NE, NE)	63.5 (55.7, 71.2)
12 months	NE (NE, NE)	57.7 (44.8, 70.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.35	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	12 (8.7)	25 (9.1)
Number of Subjects Censored, n (%)	126 (91.3)	251 (90.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.5*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.789 (0.362)
95% CI		(0.388, 1.602)
Log-rank p-value		0.597

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.1 (86.2, 95.9)	92.4 (89.2, 95.6)
6 months	91.1 (86.2, 95.9)	89.2 (84.7, 93.7)
9 months	NE (NE, NE)	87.8 (82.6, 93.0)
12 months	NE (NE, NE)	87.8 (82.6, 93.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	7 (5.1)	27 (9.8)
Number of Subjects Censored, n (%)	131 (94.9)	249 (90.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.709 (0.434)
95% CI		(0.730, 4.000)
Log-rank p-value		0.239

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.7 (90.8, 98.5)	91.9 (88.6, 95.1)
6 months	94.7 (90.8, 98.5)	89.1 (84.6, 93.6)
9 months	NE (NE, NE)	85.0 (77.9, 92.1)
12 months	NE (NE, NE)	85.0 (77.9, 92.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	1 (0.7)	15 (5.4)
Number of Subjects Censored, n (%)	137 (99.3)	261 (94.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		8.018 (1.037)
95% CI		(1.050, 61.205)
Log-rank p-value		0.016

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	94.7 (92.0, 97.4)
6 months	99.3 (97.8, 100.0)	93.7 (90.3, 97.0)
9 months	NE (NE, NE)	93.7 (90.3, 97.0)
12 months	NE (NE, NE)	93.7 (90.3, 97.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	2 (1.4)	6 (2.2)
Number of Subjects Censored, n (%)	136 (98.6)	270 (97.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.445 (0.827)
95% CI		(0.286, 7.302)
Log-rank p-value		0.718

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.3, 100.0)	97.7 (95.9, 99.5)
6 months	98.4 (96.3, 100.0)	97.7 (95.9, 99.5)
9 months	NE (NE, NE)	97.7 (95.9, 99.5)
12 months	NE (NE, NE)	97.7 (95.9, 99.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	2 (1.4)	8 (2.9)
Number of Subjects Censored, n (%)	136 (98.6)	268 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.436 (0.820)
95% CI		(0.288, 7.169)
Log-rank p-value		0.572

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.5, 100.0)	97.8 (96.0, 99.5)
6 months	98.5 (96.5, 100.0)	97.8 (96.0, 99.5)
9 months	NE (NE, NE)	93.6 (87.8, 99.5)
12 months	NE (NE, NE)	93.6 (87.8, 99.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	0	9 (3.3)
Number of Subjects Censored, n (%)	138 (100.0)	267 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.082

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.4 (94.1, 98.7)
6 months	100.0 (100.0, 100.0)	96.4 (94.1, 98.7)
9 months	NE (NE, NE)	96.4 (94.1, 98.7)
12 months	NE (NE, NE)	96.4 (94.1, 98.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	17 (12.3)	87 (31.5)
Number of Subjects Censored, n (%)	121 (87.7)	189 (68.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.61 (1.15, 2.66)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.684 (0.267)
95% CI		(1.590, 4.529)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.4 (81.8, 93.0)	69.8 (64.3, 75.4)
6 months	87.4 (81.8, 93.0)	65.8 (59.5, 72.1)
9 months	NE (NE, NE)	64.2 (57.4, 71.1)
12 months	NE (NE, NE)	64.2 (57.4, 71.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.71	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	3 (2.2)	49 (17.8)
Number of Subjects Censored, n (%)	135 (97.8)	227 (82.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.86, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.1, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		8.118 (0.597)
95% CI		(2.520, 26.146)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (95.1, 100.0)	83.5 (79.1, 88.0)
6 months	97.7 (95.1, 100.0)	78.9 (72.9, 84.8)
9 months	NE (NE, NE)	78.9 (72.9, 84.8)
12 months	NE (NE, NE)	78.9 (72.9, 84.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.10

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	5 (3.6)	12 (4.3)
Number of Subjects Censored, n (%)	133 (96.4)	264 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.066 (0.535)
95% CI		(0.374, 3.044)
Log-rank p-value		0.888

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.3 (93.2, 99.5)	95.6 (93.1, 98.0)
6 months	96.3 (93.2, 99.5)	95.6 (93.1, 98.0)
9 months	NE (NE, NE)	95.6 (93.1, 98.0)
12 months	NE (NE, NE)	95.6 (93.1, 98.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	1 (0.7)	7 (2.5)
Number of Subjects Censored, n (%)	137 (99.3)	269 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.7, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.010 (1.077)
95% CI		(0.364, 24.871)
Log-rank p-value		0.308

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	97.7 (95.8, 99.5)
6 months	99.3 (97.8, 100.0)	97.0 (94.7, 99.3)
9 months	NE (NE, NE)	97.0 (94.7, 99.3)
12 months	NE (NE, NE)	97.0 (94.7, 99.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	26 (18.8)	73 (26.4)
Number of Subjects Censored, n (%)	112 (81.2)	203 (73.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.81, NE)	4.01 (1.61, 11.10)
Median (95% CI)	NE (NE, NE)	NE (11.10, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.403 (0.232)
95% CI		(0.889, 2.212)
Log-rank p-value		0.166

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.2 (73.3, 87.1)	75.7 (70.5, 80.9)
6 months	80.2 (73.3, 87.1)	70.2 (63.7, 76.7)
9 months	NE (NE, NE)	68.8 (61.8, 75.7)
12 months	NE (NE, NE)	61.1 (45.7, 76.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.43	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	6 (4.3)	25 (9.1)
Number of Subjects Censored, n (%)	132 (95.7)	251 (90.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.254 (0.459)
95% CI		(0.917, 5.542)
Log-rank p-value		0.077

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.8 (90.7, 99.0)	91.6 (88.2, 94.9)
6 months	94.8 (90.7, 99.0)	90.7 (87.0, 94.4)
9 months	NE (NE, NE)	89.3 (84.7, 93.8)
12 months	NE (NE, NE)	89.3 (84.7, 93.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.45

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	7 (5.1)	5 (1.8)
Number of Subjects Censored, n (%)	131 (94.9)	271 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.307 (0.593)
95% CI		(0.096, 0.984)
Log-rank p-value		0.036

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (91.2, 98.6)	98.1 (96.5, 99.8)
6 months	94.9 (91.2, 98.6)	98.1 (96.5, 99.8)
9 months	NE (NE, NE)	98.1 (96.5, 99.8)
12 months	NE (NE, NE)	98.1 (96.5, 99.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	3 (2.2)	10 (3.6)
Number of Subjects Censored, n (%)	135 (97.8)	266 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.2, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.733 (0.663)
95% CI		(0.473, 6.354)
Log-rank p-value		0.410

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (94.9, 100.0)	96.3 (94.0, 98.5)
6 months	97.6 (94.9, 100.0)	96.3 (94.0, 98.5)
9 months	NE (NE, NE)	96.3 (94.0, 98.5)
12 months	NE (NE, NE)	96.3 (94.0, 98.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	16 (11.6)	58 (21.0)
Number of Subjects Censored, n (%)	122 (88.4)	218 (79.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	6.47 (3.61, NE)
Median (95% CI)	NE (NE, NE)	NE (11.96, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (11.96, NE)
Min, Max	0.0, 6.5*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.493 (0.289)
95% CI		(0.846, 2.632)
Log-rank p-value		0.176

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.0 (80.9, 93.1)	82.4 (77.7, 87.0)
6 months	87.0 (80.9, 93.1)	75.9 (70.0, 81.9)
9 months	NE (NE, NE)	72.5 (65.2, 79.8)
12 months	NE (NE, NE)	54.4 (23.1, 85.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.71	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	4 (2.9)	43 (15.6)
Number of Subjects Censored, n (%)	134 (97.1)	233 (84.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.3, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.829 (0.526)
95% CI		(1.721, 13.549)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (93.8, 99.9)	86.1 (81.9, 90.4)
6 months	96.9 (93.8, 99.9)	81.4 (76.1, 86.7)
9 months	NE (NE, NE)	81.4 (76.1, 86.7)
12 months	NE (NE, NE)	81.4 (76.1, 86.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.33

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	4 (2.9)	2 (0.7)
Number of Subjects Censored, n (%)	134 (97.1)	274 (99.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.7, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.136 (0.944)
95% CI		(0.021, 0.866)
Log-rank p-value		0.030

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (93.9, 99.9)	99.3 (98.3, 100.0)
6 months	96.9 (93.9, 99.9)	99.3 (98.3, 100.0)
9 months	NE (NE, NE)	99.3 (98.3, 100.0)
12 months	NE (NE, NE)	99.3 (98.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	10 (7.2)	51 (18.5)
Number of Subjects Censored, n (%)	128 (92.8)	225 (81.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.91 (4.63, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.793 (0.356)
95% CI		(0.893, 3.601)
Log-rank p-value		0.089

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.2 (87.5, 96.9)	87.0 (82.8, 91.1)
6 months	92.2 (87.5, 96.9)	74.2 (66.7, 81.6)
9 months	NE (NE, NE)	67.0 (56.8, 77.3)
12 months	NE (NE, NE)	67.0 (56.8, 77.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	2 (1.4)	7 (2.5)
Number of Subjects Censored, n (%)	136 (98.6)	269 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.2, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.630 (0.830)
95% CI		(0.320, 8.289)
Log-rank p-value		0.566

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.5, 100.0)	98.1 (96.5, 99.8)
6 months	98.5 (96.5, 100.0)	96.1 (93.0, 99.3)
9 months	NE (NE, NE)	96.1 (93.0, 99.3)
12 months	NE (NE, NE)	96.1 (93.0, 99.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	3 (2.2)	5 (1.8)
Number of Subjects Censored, n (%)	135 (97.8)	271 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.423 (0.801)
95% CI		(0.088, 2.033)
Log-rank p-value		0.300

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (94.4, 100.0)	99.3 (98.3, 100.0)
6 months	97.4 (94.4, 100.0)	96.4 (93.0, 99.8)
9 months	NE (NE, NE)	96.4 (93.0, 99.8)
12 months	NE (NE, NE)	96.4 (93.0, 99.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	0	9 (3.3)
Number of Subjects Censored, n (%)	138 (100.0)	267 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.057

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.8 (94.5, 99.0)
6 months	100.0 (100.0, 100.0)	95.6 (92.4, 98.8)
9 months	NE (NE, NE)	95.6 (92.4, 98.8)
12 months	NE (NE, NE)	95.6 (92.4, 98.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	20 (14.5)	36 (13.0)
Number of Subjects Censored, n (%)	118 (85.5)	240 (87.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.697 (0.287)
95% CI		(0.397, 1.222)
Log-rank p-value		0.240

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.7 (78.5, 90.9)	88.3 (84.4, 92.3)
6 months	84.7 (78.5, 90.9)	84.0 (78.6, 89.4)
9 months	NE (NE, NE)	82.5 (76.5, 88.6)
12 months	NE (NE, NE)	82.5 (76.5, 88.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	13 (9.4)	18 (6.5)
Number of Subjects Censored, n (%)	125 (90.6)	258 (93.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.469 (0.381)
95% CI		(0.222, 0.989)
Log-rank p-value		0.049

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.7 (84.4, 95.1)	95.2 (92.6, 97.9)
6 months	89.7 (84.4, 95.1)	90.9 (86.3, 95.5)
9 months	NE (NE, NE)	89.5 (84.2, 94.8)
12 months	NE (NE, NE)	89.5 (84.2, 94.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.74	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	2 (1.4)	17 (6.2)
Number of Subjects Censored, n (%)	136 (98.6)	259 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.1, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.182 (0.750)
95% CI		(0.961, 18.194)
Log-rank p-value		0.039

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.3, 100.0)	93.4 (90.3, 96.5)
6 months	98.4 (96.3, 100.0)	93.4 (90.3, 96.5)
9 months	NE (NE, NE)	93.4 (90.3, 96.5)
12 months	NE (NE, NE)	93.4 (90.3, 96.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Endocrine disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	1 (0.7)	57 (20.7)
Number of Subjects Censored, n (%)	137 (99.3)	219 (79.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.59 (3.58, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		24.299 (1.011)
95% CI		(3.351, 176.188)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Endocrine disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	82.0 (77.3, 86.8)
6 months	99.3 (97.8, 100.0)	71.4 (63.6, 79.1)
9 months	NE (NE, NE)	69.7 (61.4, 77.9)
12 months	NE (NE, NE)	69.7 (61.4, 77.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.10

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	1 (0.7)	52 (18.8)
Number of Subjects Censored, n (%)	137 (99.3)	224 (81.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.98 (4.17, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		21.777 (1.012)
95% CI		(2.996, 158.295)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	84.0 (79.5, 88.6)
6 months	99.3 (97.8, 100.0)	73.6 (66.1, 81.2)
9 months	NE (NE, NE)	72.0 (63.9, 80.0)
12 months	NE (NE, NE)	72.0 (63.9, 80.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	8 (5.8)	40 (14.5)
Number of Subjects Censored, n (%)	130 (94.2)	236 (85.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.72, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.914 (0.395)
95% CI		(0.883, 4.147)
Log-rank p-value		0.085

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.7 (89.4, 98.0)	87.0 (82.8, 91.2)
6 months	93.7 (89.4, 98.0)	81.3 (75.5, 87.1)
9 months	NE (NE, NE)	81.3 (75.5, 87.1)
12 months	NE (NE, NE)	81.3 (75.5, 87.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	6 (4.3)	18 (6.5)
Number of Subjects Censored, n (%)	132 (95.7)	258 (93.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.898 (0.487)
95% CI		(0.346, 2.331)
Log-rank p-value		0.898

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (91.8, 99.0)	93.6 (90.5, 96.8)
6 months	95.4 (91.8, 99.0)	91.5 (87.5, 95.4)
9 months	NE (NE, NE)	91.5 (87.5, 95.4)
12 months	NE (NE, NE)	91.5 (87.5, 95.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	1 (0.7)	8 (2.9)
Number of Subjects Censored, n (%)	137 (99.3)	268 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.562 (1.072)
95% CI		(0.436, 29.119)
Log-rank p-value		0.242

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.6, 100.0)	96.8 (94.6, 99.0)
6 months	99.2 (97.6, 100.0)	96.8 (94.6, 99.0)
9 months	NE (NE, NE)	96.8 (94.6, 99.0)
12 months	NE (NE, NE)	96.8 (94.6, 99.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	1 (0.7)	9 (3.3)
Number of Subjects Censored, n (%)	137 (99.3)	267 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.3, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.277 (1.068)
95% CI		(0.527, 34.702)
Log-rank p-value		0.140

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.0, 100.0)	97.3 (95.4, 99.3)
6 months	99.0 (97.0, 100.0)	95.6 (92.4, 98.7)
9 months	NE (NE, NE)	95.6 (92.4, 98.7)
12 months	NE (NE, NE)	95.6 (92.4, 98.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	13 (9.4)	32 (11.6)
Number of Subjects Censored, n (%)	125 (90.6)	244 (88.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.62, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.1, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.961 (0.338)
95% CI		(0.495, 1.865)
Log-rank p-value		0.901

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.3 (85.3, 95.3)	89.9 (86.1, 93.6)
6 months	90.3 (85.3, 95.3)	85.0 (79.5, 90.5)
9 months	NE (NE, NE)	82.9 (76.1, 89.6)
12 months	NE (NE, NE)	82.9 (76.1, 89.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	2 (1.4)	12 (4.3)
Number of Subjects Censored, n (%)	136 (98.6)	264 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.8*, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.497 (0.772)
95% CI		(0.549, 11.346)
Log-rank p-value		0.248

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.3, 100.0)	96.0 (93.5, 98.4)
6 months	98.4 (96.3, 100.0)	94.1 (90.4, 97.7)
9 months	NE (NE, NE)	94.1 (90.4, 97.7)
12 months	NE (NE, NE)	94.1 (90.4, 97.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Number of Subjects with Events, n (%)	2 (1.4)	9 (3.3)
Number of Subjects Censored, n (%)	136 (98.6)	267 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.401 (0.813)
95% CI		(0.285, 6.887)
Log-rank p-value		0.569

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Colon

Statistics	Placebo + BSC N=138	Fruquintinib + BSC N=276
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.5, 100.0)	97.8 (96.0, 99.5)
6 months	98.5 (96.5, 100.0)	95.9 (92.6, 99.1)
9 months	NE (NE, NE)	93.6 (88.2, 99.0)
12 months	NE (NE, NE)	93.6 (88.2, 99.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	30 (43.5)	98 (69.5)
Number of Subjects Censored, n (%)	39 (56.5)	43 (30.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.72 (0.49, 1.58)	0.43 (0.20, 0.66)
Median (95% CI)	4.70 (2.60, NE)	1.05 (0.69, 2.43)
75% percentile (95% CI)	NE (4.70, NE)	6.97 (4.21, NE)
Min, Max	0.0, 13.0*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.634 (0.213)
95% CI		(1.076, 2.481)
Log-rank p-value		0.016

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	58.8 (46.6, 70.9)	36.4 (28.4, 44.5)
6 months	41.7 (22.1, 61.4)	28.7 (20.6, 36.9)
9 months	41.7 (22.1, 61.4)	23.3 (13.7, 33.0)
12 months	41.7 (22.1, 61.4)	23.3 (13.7, 33.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	1.05

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	13 (18.8)	51 (36.2)
Number of Subjects Censored, n (%)	56 (81.2)	90 (63.8)
Time to first TEAE (months)		
25% percentile (95% CI)	4.70 (2.60, NE)	0.99 (0.69, 2.53)
Median (95% CI)	NE (4.70, NE)	NE (8.41, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.687 (0.314)
95% CI		(0.911, 3.124)
Log-rank p-value		0.072

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.9 (71.9, 91.8)	65.9 (58.0, 73.9)
6 months	69.3 (50.0, 88.6)	64.0 (55.8, 72.1)
9 months	69.3 (50.0, 88.6)	57.6 (45.9, 69.3)
12 months	69.3 (50.0, 88.6)	57.6 (45.9, 69.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	8 (11.6)	29 (20.6)
Number of Subjects Censored, n (%)	61 (88.4)	112 (79.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.60, NE)	NE (2.33, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.768 (0.415)
95% CI		(0.784, 3.989)
Log-rank p-value		0.204

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.0 (76.8, 95.3)	81.1 (74.5, 87.7)
6 months	86.0 (76.8, 95.3)	78.1 (70.6, 85.7)
9 months	86.0 (76.8, 95.3)	75.6 (66.8, 84.4)
12 months	86.0 (76.8, 95.3)	75.6 (66.8, 84.4)
18 months	NE (NE, NE)	75.6 (66.8, 84.4)
Median Follow-up Time (months)	2.60	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	8 (11.6)	11 (7.8)
Number of Subjects Censored, n (%)	61 (88.4)	130 (92.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.70, NE)	11.53 (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.503 (0.482)
95% CI		(0.196, 1.292)
Log-rank p-value		0.147

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.4 (82.0, 96.9)	93.6 (89.5, 97.6)
6 months	79.5 (60.0, 99.0)	91.9 (86.8, 97.0)
9 months	79.5 (60.0, 99.0)	91.9 (86.8, 97.0)
12 months	79.5 (60.0, 99.0)	73.5 (41.0, 100.0)
18 months	NE (NE, NE)	73.5 (41.0, 100.0)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	0	16 (11.3)
Number of Subjects Censored, n (%)	69 (100.0)	125 (88.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
Median (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.24, NE)
Min, Max	0.2*, 13.0*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.008

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	89.0 (83.7, 94.3)
6 months	100.0 (100.0, 100.0)	89.0 (83.7, 94.3)
9 months	100.0 (100.0, 100.0)	89.0 (83.7, 94.3)
12 months	100.0 (100.0, 100.0)	89.0 (83.7, 94.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	6 (8.7)	8 (5.7)
Number of Subjects Censored, n (%)	63 (91.3)	133 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.599 (0.563)
95% CI		(0.199, 1.806)
Log-rank p-value		0.422

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (83.9, 97.8)	95.6 (92.1, 99.0)
6 months	90.9 (83.9, 97.8)	93.2 (88.5, 97.9)
9 months	90.9 (83.9, 97.8)	93.2 (88.5, 97.9)
12 months	90.9 (83.9, 97.8)	93.2 (88.5, 97.9)
18 months	NE (NE, NE)	93.2 (88.5, 97.9)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	3 (4.3)	5 (3.5)
Number of Subjects Censored, n (%)	66 (95.7)	136 (96.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.99, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.397 (0.787)
95% CI		(0.085, 1.856)
Log-rank p-value		0.156

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (90.4, 100.0)	97.7 (95.0, 100.0)
6 months	95.4 (90.4, 100.0)	97.7 (95.0, 100.0)
9 months	95.4 (90.4, 100.0)	93.0 (83.8, 100.0)
12 months	95.4 (90.4, 100.0)	86.4 (71.2, 100.0)
18 months	NE (NE, NE)	86.4 (71.2, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	0	6 (4.3)
Number of Subjects Censored, n (%)	69 (100.0)	135 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.00, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.200

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.9 (95.5, 100.0)
6 months	100.0 (100.0, 100.0)	97.9 (95.5, 100.0)
9 months	100.0 (100.0, 100.0)	97.9 (95.5, 100.0)
12 months	100.0 (100.0, 100.0)	80.6 (62.5, 98.6)
18 months	NE (NE, NE)	80.6 (62.5, 98.6)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	2 (2.9)	3 (2.1)
Number of Subjects Censored, n (%)	67 (97.1)	138 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.493 (0.931)
95% CI		(0.080, 3.060)
Log-rank p-value		0.403

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.7 (92.1, 100.0)	98.4 (96.2, 100.0)
6 months	96.7 (92.1, 100.0)	97.1 (93.8, 100.0)
9 months	96.7 (92.1, 100.0)	97.1 (93.8, 100.0)
12 months	96.7 (92.1, 100.0)	97.1 (93.8, 100.0)
18 months	NE (NE, NE)	97.1 (93.8, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	1 (1.4)	3 (2.1)
Number of Subjects Censored, n (%)	68 (98.6)	138 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.013 (1.167)
95% CI		(0.103, 9.983)
Log-rank p-value		0.991

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.7, 100.0)	98.5 (96.5, 100.0)
6 months	98.5 (95.7, 100.0)	98.5 (96.5, 100.0)
9 months	98.5 (95.7, 100.0)	94.3 (85.8, 100.0)
12 months	98.5 (95.7, 100.0)	94.3 (85.8, 100.0)
18 months	NE (NE, NE)	94.3 (85.8, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	39 (56.5)	86 (61.0)
Number of Subjects Censored, n (%)	30 (43.5)	55 (39.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.13, 0.72)	0.59 (0.36, 0.69)
Median (95% CI)	1.84 (0.92, 4.34)	1.87 (1.02, 4.40)
75% percentile (95% CI)	5.59 (4.34, NE)	NE (6.70, NE)
Min, Max	0.0, 6.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.869 (0.201)
95% CI		(0.586, 1.288)
Log-rank p-value		0.448

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	44.8 (32.6, 57.1)	45.9 (37.5, 54.2)
6 months	19.9 (0.0, 40.7)	36.0 (26.9, 45.1)
9 months	NE (NE, NE)	26.0 (14.2, 37.7)
12 months	NE (NE, NE)	26.0 (14.2, 37.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.31	1.74

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	5 (7.2)	30 (21.3)
Number of Subjects Censored, n (%)	64 (92.8)	111 (78.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	6.47 (2.89, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.278 (0.492)
95% CI		(0.869, 5.970)
Log-rank p-value		0.108

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.4 (85.9, 98.8)	82.3 (75.9, 88.8)
6 months	92.4 (85.9, 98.8)	76.2 (67.7, 84.7)
9 months	92.4 (85.9, 98.8)	71.4 (61.2, 81.6)
12 months	92.4 (85.9, 98.8)	71.4 (61.2, 81.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	10 (14.5)	24 (17.0)
Number of Subjects Censored, n (%)	59 (85.5)	117 (83.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	9.00 (5.03, NE)
Median (95% CI)	NE (4.34, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.789 (0.394)
95% CI		(0.365, 1.705)
Log-rank p-value		0.584

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.2 (77.7, 94.6)	87.3 (81.6, 93.0)
6 months	75.4 (54.3, 96.5)	80.2 (72.1, 88.2)
9 months	75.4 (54.3, 96.5)	78.2 (69.4, 86.9)
12 months	75.4 (54.3, 96.5)	73.8 (62.1, 85.5)
18 months	NE (NE, NE)	73.8 (62.1, 85.5)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	10 (14.5)	20 (14.2)
Number of Subjects Censored, n (%)	59 (85.5)	121 (85.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.57, NE)	NE (5.52, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.784 (0.405)
95% CI		(0.354, 1.735)
Log-rank p-value		0.708

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.2 (77.7, 94.6)	88.7 (83.3, 94.2)
6 months	77.6 (59.8, 95.3)	83.0 (75.6, 90.5)
9 months	77.6 (59.8, 95.3)	81.1 (72.9, 89.3)
12 months	77.6 (59.8, 95.3)	81.1 (72.9, 89.3)
18 months	NE (NE, NE)	81.1 (72.9, 89.3)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	4 (5.8)	16 (11.3)
Number of Subjects Censored, n (%)	65 (94.2)	125 (88.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.70, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.162 (0.579)
95% CI		(0.374, 3.610)
Log-rank p-value		0.833

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (90.7, 100.0)	92.0 (87.1, 96.8)
6 months	91.8 (83.0, 100.0)	87.6 (80.8, 94.4)
9 months	91.8 (83.0, 100.0)	82.1 (72.3, 91.8)
12 months	91.8 (83.0, 100.0)	76.2 (61.9, 90.5)
18 months	NE (NE, NE)	76.2 (61.9, 90.5)
Median Follow-up Time (months)	2.83	3.98

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	7 (10.1)	22 (15.6)
Number of Subjects Censored, n (%)	62 (89.9)	119 (84.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.52, NE)	18.04 (5.82, NE)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.1, 13.0*	0.1, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.970 (0.449)
95% CI		(0.403, 2.338)
Log-rank p-value		0.874

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.7 (83.7, 97.8)	89.1 (83.9, 94.3)
6 months	85.7 (74.0, 97.4)	83.4 (76.0, 90.8)
9 months	85.7 (74.0, 97.4)	79.6 (71.0, 88.3)
12 months	85.7 (74.0, 97.4)	79.6 (71.0, 88.3)
18 months	NE (NE, NE)	79.6 (71.0, 88.3)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	3 (4.3)	18 (12.8)
Number of Subjects Censored, n (%)	66 (95.7)	123 (87.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.600 (0.629)
95% CI		(0.758, 8.919)
Log-rank p-value		0.129

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.8 (89.2, 100.0)	87.7 (82.2, 93.2)
6 months	94.8 (89.2, 100.0)	86.7 (80.9, 92.4)
9 months	94.8 (89.2, 100.0)	86.7 (80.9, 92.4)
12 months	94.8 (89.2, 100.0)	86.7 (80.9, 92.4)
18 months	NE (NE, NE)	86.7 (80.9, 92.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	2 (2.9)	6 (4.3)
Number of Subjects Censored, n (%)	67 (97.1)	135 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.4*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.732 (0.875)
95% CI		(0.132, 4.071)
Log-rank p-value		0.645

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (95.2, 100.0)	97.1 (94.3, 99.9)
6 months	84.3 (58.7, 100.0)	95.3 (90.9, 99.8)
9 months	NE (NE, NE)	92.1 (84.7, 99.6)
12 months	NE (NE, NE)	92.1 (84.7, 99.6)
18 months	NE (NE, NE)	92.1 (84.7, 99.6)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	2 (2.9)	9 (6.4)
Number of Subjects Censored, n (%)	67 (97.1)	132 (93.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.131 (0.941)
95% CI		(0.337, 13.473)
Log-rank p-value		0.534

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.8 (92.4, 100.0)	95.7 (92.3, 99.1)
6 months	96.8 (92.4, 100.0)	92.6 (87.2, 98.0)
9 months	96.8 (92.4, 100.0)	89.6 (81.9, 97.4)
12 months	96.8 (92.4, 100.0)	89.6 (81.9, 97.4)
18 months	NE (NE, NE)	89.6 (81.9, 97.4)
Median Follow-up Time (months)	2.83	4.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	0	2 (1.4)
Number of Subjects Censored, n (%)	69 (100.0)	139 (98.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.296

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.6 (96.6, 100.0)
6 months	100.0 (100.0, 100.0)	98.6 (96.6, 100.0)
9 months	100.0 (100.0, 100.0)	98.6 (96.6, 100.0)
12 months	100.0 (100.0, 100.0)	98.6 (96.6, 100.0)
18 months	NE (NE, NE)	98.6 (96.6, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	1 (1.4)	0
Number of Subjects Censored, n (%)	68 (98.6)	141 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.061

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.5, 100.0)	100.0 (100.0, 100.0)
6 months	98.5 (95.5, 100.0)	100.0 (100.0, 100.0)
9 months	98.5 (95.5, 100.0)	100.0 (100.0, 100.0)
12 months	98.5 (95.5, 100.0)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	0	2 (1.4)
Number of Subjects Censored, n (%)	69 (100.0)	139 (98.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.353

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.5 (96.6, 100.0)
6 months	100.0 (100.0, 100.0)	98.5 (96.6, 100.0)
9 months	100.0 (100.0, 100.0)	98.5 (96.6, 100.0)
12 months	100.0 (100.0, 100.0)	98.5 (96.6, 100.0)
18 months	NE (NE, NE)	98.5 (96.6, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	13 (18.8)	60 (42.6)
Number of Subjects Censored, n (%)	56 (81.2)	81 (57.4)
Time to first TEAE (months)		
25% percentile (95% CI)	4.27 (2.04, NE)	1.64 (0.95, 2.53)
Median (95% CI)	10.18 (4.27, NE)	6.24 (3.71, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.1, 10.2	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.813 (0.310)
95% CI		(0.987, 3.331)
Log-rank p-value		0.048

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.5 (75.5, 93.4)	61.7 (53.4, 70.1)
6 months	71.5 (52.1, 90.9)	50.0 (39.9, 60.1)
9 months	71.5 (52.1, 90.9)	48.1 (37.7, 58.5)
12 months	0.0 (NE, NE)	48.1 (37.7, 58.5)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	7 (10.1)	38 (27.0)
Number of Subjects Censored, n (%)	62 (89.9)	103 (73.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.27, NE)	3.09 (1.68, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.188 (0.416)
95% CI		(0.969, 4.942)
Log-rank p-value		0.056

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (84.0, 97.9)	75.2 (67.8, 82.6)
6 months	82.7 (66.0, 99.3)	71.5 (63.4, 79.7)
9 months	82.7 (66.0, 99.3)	67.1 (57.3, 76.9)
12 months	82.7 (66.0, 99.3)	67.1 (57.3, 76.9)
18 months	NE (NE, NE)	67.1 (57.3, 76.9)
Median Follow-up Time (months)	2.83	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	1 (1.4)	6 (4.3)
Number of Subjects Censored, n (%)	68 (98.6)	135 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.386 (1.087)
95% CI		(0.284, 20.069)
Log-rank p-value		0.440

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (95.7, 100.0)	95.2 (91.4, 99.0)
6 months	98.6 (95.7, 100.0)	95.2 (91.4, 99.0)
9 months	98.6 (95.7, 100.0)	95.2 (91.4, 99.0)
12 months	98.6 (95.7, 100.0)	95.2 (91.4, 99.0)
18 months	NE (NE, NE)	95.2 (91.4, 99.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	1 (1.4)	3 (2.1)
Number of Subjects Censored, n (%)	68 (98.6)	138 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.22, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.992 (1.173)
95% CI		(0.100, 9.893)
Log-rank p-value		0.982

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.5 (96.5, 100.0)
6 months	95.8 (87.8, 100.0)	97.2 (94.0, 100.0)
9 months	95.8 (87.8, 100.0)	97.2 (94.0, 100.0)
12 months	95.8 (87.8, 100.0)	97.2 (94.0, 100.0)
18 months	NE (NE, NE)	97.2 (94.0, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	1 (1.4)	3 (2.1)
Number of Subjects Censored, n (%)	68 (98.6)	138 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.842 (1.228)
95% CI		(0.076, 9.339)
Log-rank p-value		0.853

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.9 (93.7, 100.0)	97.7 (95.2, 100.0)
6 months	97.9 (93.7, 100.0)	97.7 (95.2, 100.0)
9 months	97.9 (93.7, 100.0)	97.7 (95.2, 100.0)
12 months	97.9 (93.7, 100.0)	97.7 (95.2, 100.0)
18 months	NE (NE, NE)	97.7 (95.2, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	1 (1.4)	4 (2.8)
Number of Subjects Censored, n (%)	68 (98.6)	137 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.186 (1.141)
95% CI		(0.127, 11.099)
Log-rank p-value		0.906

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.5, 100.0)	97.7 (95.1, 100.0)
6 months	98.5 (95.5, 100.0)	96.0 (91.8, 100.0)
9 months	98.5 (95.5, 100.0)	96.0 (91.8, 100.0)
12 months	98.5 (95.5, 100.0)	96.0 (91.8, 100.0)
18 months	NE (NE, NE)	96.0 (91.8, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	0	5 (3.5)
Number of Subjects Censored, n (%)	69 (100.0)	136 (96.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.295

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.7 (95.1, 100.0)
6 months	100.0 (100.0, 100.0)	95.8 (91.3, 100.0)
9 months	100.0 (100.0, 100.0)	93.1 (86.2, 99.9)
12 months	100.0 (100.0, 100.0)	93.1 (86.2, 99.9)
18 months	NE (NE, NE)	93.1 (86.2, 99.9)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	0	3 (2.1)
Number of Subjects Censored, n (%)	69 (100.0)	138 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.252

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.7 (95.1, 100.0)
6 months	100.0 (100.0, 100.0)	97.7 (95.1, 100.0)
9 months	100.0 (100.0, 100.0)	97.7 (95.1, 100.0)
12 months	100.0 (100.0, 100.0)	97.7 (95.1, 100.0)
18 months	NE (NE, NE)	97.7 (95.1, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	1 (1.4)	3 (2.1)
Number of Subjects Censored, n (%)	68 (98.6)	138 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.303 (1.155)
95% CI		(0.135, 12.545)
Log-rank p-value		0.798

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.5, 100.0)	97.8 (95.3, 100.0)
6 months	98.5 (95.5, 100.0)	97.8 (95.3, 100.0)
9 months	98.5 (95.5, 100.0)	97.8 (95.3, 100.0)
12 months	98.5 (95.5, 100.0)	97.8 (95.3, 100.0)
18 months	NE (NE, NE)	97.8 (95.3, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	2 (2.9)	4 (2.8)
Number of Subjects Censored, n (%)	67 (97.1)	137 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Median (95% CI)	10.18 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 10.2	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.593 (0.883)
95% CI		(0.105, 3.345)
Log-rank p-value		0.575

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.5, 100.0)	97.1 (94.4, 99.9)
6 months	98.5 (95.5, 100.0)	97.1 (94.4, 99.9)
9 months	98.5 (95.5, 100.0)	97.1 (94.4, 99.9)
12 months	0.0 (NE, NE)	97.1 (94.4, 99.9)
18 months	0.0 (NE, NE)	97.1 (94.4, 99.9)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	0	2 (1.4)
Number of Subjects Censored, n (%)	69 (100.0)	139 (98.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.492

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.3 (97.9, 100.0)
6 months	100.0 (100.0, 100.0)	97.4 (93.6, 100.0)
9 months	100.0 (100.0, 100.0)	97.4 (93.6, 100.0)
12 months	100.0 (100.0, 100.0)	97.4 (93.6, 100.0)
18 months	NE (NE, NE)	97.4 (93.6, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	19 (27.5)	57 (40.4)
Number of Subjects Censored, n (%)	50 (72.5)	84 (59.6)
Time to first TEAE (months)		
25% percentile (95% CI)	3.55 (0.69, 5.59)	1.64 (0.95, 2.69)
Median (95% CI)	NE (3.71, NE)	7.16 (4.73, NE)
75% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Min, Max	0.2*, 6.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.098 (0.276)
95% CI		(0.639, 1.886)
Log-rank p-value		0.615

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.7 (65.3, 86.1)	65.1 (56.9, 73.2)
6 months	50.8 (24.4, 77.2)	54.2 (44.5, 64.0)
9 months	NE (NE, NE)	49.9 (39.1, 60.6)
12 months	NE (NE, NE)	49.9 (39.1, 60.6)
18 months	NE (NE, NE)	49.9 (39.1, 60.6)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	6 (8.7)	17 (12.1)
Number of Subjects Censored, n (%)	63 (91.3)	124 (87.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (6.47, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.970 (0.492)
95% CI		(0.370, 2.543)
Log-rank p-value		0.893

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.0 (83.2, 98.7)	89.3 (84.0, 94.7)
6 months	78.0 (53.5, 100.0)	86.1 (79.3, 92.9)
9 months	NE (NE, NE)	84.2 (76.7, 91.8)
12 months	NE (NE, NE)	84.2 (76.7, 91.8)
18 months	NE (NE, NE)	84.2 (76.7, 91.8)
Median Follow-up Time (months)	2.79	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	3 (4.3)	12 (8.5)
Number of Subjects Censored, n (%)	66 (95.7)	129 (91.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.245 (0.670)
95% CI		(0.335, 4.629)
Log-rank p-value		0.640

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.0 (92.8, 100.0)	91.9 (87.0, 96.8)
6 months	83.1 (57.7, 100.0)	89.5 (83.7, 95.3)
9 months	NE (NE, NE)	89.5 (83.7, 95.3)
12 months	NE (NE, NE)	89.5 (83.7, 95.3)
18 months	NE (NE, NE)	89.5 (83.7, 95.3)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	3 (4.3)	14 (9.9)
Number of Subjects Censored, n (%)	66 (95.7)	127 (90.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.148 (0.676)
95% CI		(0.305, 4.317)
Log-rank p-value		0.643

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (92.8, 100.0)	92.9 (88.4, 97.4)
6 months	83.1 (57.7, 100.0)	87.5 (80.8, 94.2)
9 months	NE (NE, NE)	85.5 (77.8, 93.1)
12 months	NE (NE, NE)	85.5 (77.8, 93.1)
18 months	NE (NE, NE)	85.5 (77.8, 93.1)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	3 (4.3)	9 (6.4)
Number of Subjects Censored, n (%)	66 (95.7)	132 (93.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.844 (0.692)
95% CI		(0.217, 3.279)
Log-rank p-value		0.834

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (90.4, 100.0)	95.5 (92.1, 99.0)
6 months	95.4 (90.4, 100.0)	92.0 (86.8, 97.2)
9 months	95.4 (90.4, 100.0)	92.0 (86.8, 97.2)
12 months	95.4 (90.4, 100.0)	92.0 (86.8, 97.2)
18 months	NE (NE, NE)	92.0 (86.8, 97.2)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	1 (1.4)	13 (9.2)
Number of Subjects Censored, n (%)	68 (98.6)	128 (90.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.326 (1.071)
95% CI		(0.775, 51.629)
Log-rank p-value		0.056

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.5, 100.0)	90.8 (85.9, 95.8)
6 months	98.5 (95.5, 100.0)	89.0 (83.0, 95.0)
9 months	98.5 (95.5, 100.0)	89.0 (83.0, 95.0)
12 months	98.5 (95.5, 100.0)	89.0 (83.0, 95.0)
18 months	NE (NE, NE)	89.0 (83.0, 95.0)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	3 (4.3)	4 (2.8)
Number of Subjects Censored, n (%)	66 (95.7)	137 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.362 (0.813)
95% CI		(0.074, 1.783)
Log-rank p-value		0.237

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (89.1, 100.0)	96.8 (93.7, 99.9)
6 months	94.9 (89.1, 100.0)	96.8 (93.7, 99.9)
9 months	94.9 (89.1, 100.0)	96.8 (93.7, 99.9)
12 months	94.9 (89.1, 100.0)	96.8 (93.7, 99.9)
18 months	NE (NE, NE)	96.8 (93.7, 99.9)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	1 (1.4)	5 (3.5)
Number of Subjects Censored, n (%)	68 (98.6)	136 (96.5)
Time to first TEAE (months)		
25% percentile (95% CI)	7.43 (NE, NE)	NE (NE, NE)
Median (95% CI)	7.43 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	7.43 (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 7.4	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.909 (1.117)
95% CI		(0.214, 17.038)
Log-rank p-value		0.525

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.3 (93.1, 99.5)
6 months	100.0 (100.0, 100.0)	96.3 (93.1, 99.5)
9 months	0.0 (NE, NE)	96.3 (93.1, 99.5)
12 months	0.0 (NE, NE)	96.3 (93.1, 99.5)
18 months	0.0 (NE, NE)	96.3 (93.1, 99.5)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	3 (4.3)	8 (5.7)
Number of Subjects Censored, n (%)	66 (95.7)	133 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.55, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.693 (0.712)
95% CI		(0.172, 2.799)
Log-rank p-value		0.561

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.4 (91.4, 100.0)	96.3 (93.0, 99.5)
6 months	90.7 (79.0, 100.0)	92.0 (86.4, 97.7)
9 months	90.7 (79.0, 100.0)	92.0 (86.4, 97.7)
12 months	90.7 (79.0, 100.0)	92.0 (86.4, 97.7)
18 months	NE (NE, NE)	92.0 (86.4, 97.7)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	1 (1.4)	1 (0.7)
Number of Subjects Censored, n (%)	68 (98.6)	140 (99.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.448 (1.415)
95% CI		(0.028, 7.169)
Log-rank p-value		0.557

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.5, 100.0)	99.3 (97.9, 100.0)
6 months	98.5 (95.5, 100.0)	99.3 (97.9, 100.0)
9 months	98.5 (95.5, 100.0)	99.3 (97.9, 100.0)
12 months	98.5 (95.5, 100.0)	99.3 (97.9, 100.0)
18 months	NE (NE, NE)	99.3 (97.9, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	1 (1.4)	2 (1.4)
Number of Subjects Censored, n (%)	68 (98.6)	139 (98.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.798 (1.228)
95% CI		(0.072, 8.855)
Log-rank p-value		0.834

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.5, 100.0)	98.4 (96.2, 100.0)
6 months	98.5 (95.5, 100.0)	98.4 (96.2, 100.0)
9 months	98.5 (95.5, 100.0)	98.4 (96.2, 100.0)
12 months	98.5 (95.5, 100.0)	98.4 (96.2, 100.0)
18 months	NE (NE, NE)	98.4 (96.2, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	16 (23.2)	53 (37.6)
Number of Subjects Censored, n (%)	53 (76.8)	88 (62.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.43, NE)	1.58 (0.69, 2.00)
Median (95% CI)	NE (NE, NE)	11.53 (6.41, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.533 (0.295)
95% CI		(0.860, 2.732)
Log-rank p-value		0.194

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.4 (64.7, 86.0)	67.5 (59.6, 75.3)
6 months	75.4 (64.7, 86.0)	60.2 (50.9, 69.5)
9 months	75.4 (64.7, 86.0)	55.8 (45.3, 66.2)
12 months	75.4 (64.7, 86.0)	46.5 (27.7, 65.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	5 (7.2)	22 (15.6)
Number of Subjects Censored, n (%)	64 (92.8)	119 (84.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.265 (0.507)
95% CI		(0.839, 6.115)
Log-rank p-value		0.105

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.4 (86.0, 98.8)	84.2 (78.1, 90.3)
6 months	92.4 (86.0, 98.8)	84.2 (78.1, 90.3)
9 months	92.4 (86.0, 98.8)	84.2 (78.1, 90.3)
12 months	92.4 (86.0, 98.8)	84.2 (78.1, 90.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	4 (5.8)	10 (7.1)
Number of Subjects Censored, n (%)	65 (94.2)	131 (92.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	14.32 (10.28, NE)
Median (95% CI)	NE (NE, NE)	NE (14.32, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (14.32, NE)
Min, Max	0.0, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.824 (0.660)
95% CI		(0.226, 3.005)
Log-rank p-value		0.524

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.7 (87.7, 99.7)	96.3 (93.1, 99.5)
6 months	93.7 (87.7, 99.7)	93.2 (88.0, 98.5)
9 months	93.7 (87.7, 99.7)	91.4 (85.1, 97.6)
12 months	93.7 (87.7, 99.7)	84.3 (69.9, 98.8)
18 months	NE (NE, NE)	56.2 (10.2, 100.0)
Median Follow-up Time (months)	2.79	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	7 (10.1)	13 (9.2)
Number of Subjects Censored, n (%)	62 (89.9)	128 (90.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.691 (0.497)
95% CI		(0.261, 1.829)
Log-rank p-value		0.488

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.5 (80.4, 96.7)	92.8 (88.5, 97.1)
6 months	88.5 (80.4, 96.7)	91.4 (86.4, 96.4)
9 months	88.5 (80.4, 96.7)	89.4 (83.2, 95.7)
12 months	88.5 (80.4, 96.7)	76.7 (52.9, 100.0)
18 months	NE (NE, NE)	76.7 (52.9, 100.0)
Median Follow-up Time (months)	2.60	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	1 (1.4)	7 (5.0)
Number of Subjects Censored, n (%)	68 (98.6)	134 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.6, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.550 (1.071)
95% CI		(0.435, 28.953)
Log-rank p-value		0.212

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (95.7, 100.0)	94.8 (91.1, 98.6)
6 months	98.6 (95.7, 100.0)	94.8 (91.1, 98.6)
9 months	98.6 (95.7, 100.0)	94.8 (91.1, 98.6)
12 months	98.6 (95.7, 100.0)	94.8 (91.1, 98.6)
18 months	NE (NE, NE)	94.8 (91.1, 98.6)
Median Follow-up Time (months)	2.83	4.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	1 (1.4)	4 (2.8)
Number of Subjects Censored, n (%)	68 (98.6)	137 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.459 (1.146)
95% CI		(0.154, 13.802)
Log-rank p-value		0.764

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.6, 100.0)	97.9 (95.5, 100.0)
6 months	98.5 (95.6, 100.0)	97.9 (95.5, 100.0)
9 months	98.5 (95.6, 100.0)	95.4 (90.0, 100.0)
12 months	98.5 (95.6, 100.0)	95.4 (90.0, 100.0)
18 months	NE (NE, NE)	95.4 (90.0, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Vascular disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	8 (11.6)	55 (39.0)
Number of Subjects Censored, n (%)	61 (88.4)	86 (61.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.14, NE)	0.85 (0.62, 1.87)
Median (95% CI)	NE (NE, NE)	NE (6.93, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.4*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.265 (0.382)
95% CI		(1.544, 6.906)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Vascular disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.5 (77.7, 95.4)	62.8 (54.6, 70.9)
6 months	86.5 (77.7, 95.4)	59.8 (51.0, 68.5)
9 months	NE (NE, NE)	52.9 (40.9, 64.8)
12 months	NE (NE, NE)	52.9 (40.9, 64.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	6 (8.7)	53 (37.6)
Number of Subjects Censored, n (%)	63 (91.3)	88 (62.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.95 (0.62, 1.91)
Median (95% CI)	NE (NE, NE)	NE (6.93, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.4*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.073 (0.434)
95% CI		(1.739, 9.540)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (82.3, 97.7)	64.2 (56.1, 72.3)
6 months	90.0 (82.3, 97.7)	61.1 (52.4, 69.9)
9 months	NE (NE, NE)	54.1 (42.0, 66.2)
12 months	NE (NE, NE)	54.1 (42.0, 66.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	14 (20.3)	54 (38.3)
Number of Subjects Censored, n (%)	55 (79.7)	87 (61.7)
Time to first TEAE (months)		
25% percentile (95% CI)	3.71 (1.87, NE)	1.38 (0.79, 2.50)
Median (95% CI)	NE (3.71, NE)	NE (5.75, NE)
75% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Min, Max	0.0, 6.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.572 (0.306)
95% CI		(0.863, 2.863)
Log-rank p-value		0.094

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.2 (70.8, 91.5)	63.8 (55.6, 71.9)
6 months	51.5 (19.3, 83.7)	59.5 (50.4, 68.6)
9 months	NE (NE, NE)	50.2 (35.8, 64.6)
12 months	NE (NE, NE)	50.2 (35.8, 64.6)
18 months	NE (NE, NE)	50.2 (35.8, 64.6)
Median Follow-up Time (months)	2.79	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	3 (4.3)	14 (9.9)
Number of Subjects Censored, n (%)	66 (95.7)	127 (90.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.469 (0.649)
95% CI		(0.412, 5.242)
Log-rank p-value		0.558

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.2 (89.8, 100.0)	90.0 (84.9, 95.2)
6 months	95.2 (89.8, 100.0)	88.9 (83.3, 94.4)
9 months	95.2 (89.8, 100.0)	88.9 (83.3, 94.4)
12 months	95.2 (89.8, 100.0)	88.9 (83.3, 94.4)
18 months	NE (NE, NE)	88.9 (83.3, 94.4)
Median Follow-up Time (months)	2.79	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	3 (4.3)	23 (16.3)
Number of Subjects Censored, n (%)	66 (95.7)	118 (83.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (5.32, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.899 (0.618)
95% CI		(0.863, 9.742)
Log-rank p-value		0.079

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.0 (92.9, 100.0)	84.8 (78.6, 91.0)
6 months	83.1 (57.7, 100.0)	81.8 (74.5, 89.1)
9 months	NE (NE, NE)	78.5 (69.1, 88.0)
12 months	NE (NE, NE)	78.5 (69.1, 88.0)
18 months	NE (NE, NE)	78.5 (69.1, 88.0)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	3 (4.3)	8 (5.7)
Number of Subjects Censored, n (%)	66 (95.7)	133 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.064 (0.688)
95% CI		(0.276, 4.101)
Log-rank p-value		0.840

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (95.7, 100.0)	94.1 (90.1, 98.1)
6 months	87.0 (71.7, 100.0)	94.1 (90.1, 98.1)
9 months	87.0 (71.7, 100.0)	94.1 (90.1, 98.1)
12 months	87.0 (71.7, 100.0)	94.1 (90.1, 98.1)
18 months	NE (NE, NE)	94.1 (90.1, 98.1)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	1 (1.4)	7 (5.0)
Number of Subjects Censored, n (%)	68 (98.6)	134 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.431 (1.081)
95% CI		(0.292, 20.242)
Log-rank p-value		0.374

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.5, 100.0)	95.5 (91.9, 99.0)
6 months	98.5 (95.5, 100.0)	93.5 (88.4, 98.7)
9 months	98.5 (95.5, 100.0)	93.5 (88.4, 98.7)
12 months	98.5 (95.5, 100.0)	93.5 (88.4, 98.7)
18 months	NE (NE, NE)	93.5 (88.4, 98.7)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	0	3 (2.1)
Number of Subjects Censored, n (%)	69 (100.0)	138 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.400

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.3 (97.9, 100.0)
6 months	100.0 (100.0, 100.0)	97.5 (93.8, 100.0)
9 months	100.0 (100.0, 100.0)	93.1 (83.9, 100.0)
12 months	100.0 (100.0, 100.0)	93.1 (83.9, 100.0)
18 months	NE (NE, NE)	93.1 (83.9, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	0	1 (0.7)
Number of Subjects Censored, n (%)	69 (100.0)	140 (99.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.522

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.3 (97.8, 100.0)
6 months	100.0 (100.0, 100.0)	99.3 (97.8, 100.0)
9 months	100.0 (100.0, 100.0)	99.3 (97.8, 100.0)
12 months	100.0 (100.0, 100.0)	99.3 (97.8, 100.0)
18 months	NE (NE, NE)	99.3 (97.8, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	8 (11.6)	58 (41.1)
Number of Subjects Censored, n (%)	61 (88.4)	83 (58.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.05 (0.53, 1.61)
Median (95% CI)	NE (NE, NE)	13.14 (4.90, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.14, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.119 (0.402)
95% CI		(1.872, 9.065)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.8 (79.9, 95.8)	60.9 (52.6, 69.2)
6 months	87.8 (79.9, 95.8)	55.6 (46.0, 65.3)
9 months	87.8 (79.9, 95.8)	52.5 (41.7, 63.4)
12 months	87.8 (79.9, 95.8)	52.5 (41.7, 63.4)
18 months	NE (NE, NE)	26.3 (0.0, 63.1)
Median Follow-up Time (months)	2.60	2.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	3 (4.3)	31 (22.0)
Number of Subjects Censored, n (%)	66 (95.7)	110 (78.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	7.39 (1.61, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.318 (0.625)
95% CI		(1.563, 18.091)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (90.8, 100.0)	79.7 (72.9, 86.4)
6 months	95.6 (90.8, 100.0)	76.9 (69.4, 84.4)
9 months	95.6 (90.8, 100.0)	73.9 (64.5, 83.2)
12 months	95.6 (90.8, 100.0)	73.9 (64.5, 83.2)
18 months	NE (NE, NE)	73.9 (64.5, 83.2)
Median Follow-up Time (months)	2.79	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	3 (4.3)	6 (4.3)
Number of Subjects Censored, n (%)	66 (95.7)	135 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.907 (0.720)
95% CI		(0.221, 3.716)
Log-rank p-value		0.913

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (90.4, 100.0)	95.4 (91.9, 99.0)
6 months	95.4 (90.4, 100.0)	95.4 (91.9, 99.0)
9 months	95.4 (90.4, 100.0)	95.4 (91.9, 99.0)
12 months	95.4 (90.4, 100.0)	95.4 (91.9, 99.0)
18 months	NE (NE, NE)	95.4 (91.9, 99.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	1 (1.4)	6 (4.3)
Number of Subjects Censored, n (%)	68 (98.6)	135 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.260 (1.085)
95% CI		(0.270, 18.934)
Log-rank p-value		0.439

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (95.0, 100.0)	95.6 (92.2, 99.1)
6 months	98.3 (95.0, 100.0)	95.6 (92.2, 99.1)
9 months	98.3 (95.0, 100.0)	95.6 (92.2, 99.1)
12 months	98.3 (95.0, 100.0)	95.6 (92.2, 99.1)
18 months	NE (NE, NE)	95.6 (92.2, 99.1)
Median Follow-up Time (months)	2.83	4.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	8 (11.6)	35 (24.8)
Number of Subjects Censored, n (%)	61 (88.4)	106 (75.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.63 (2.56, NE)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.2, 13.0*	0.0, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.913 (0.413)
95% CI		(0.852, 4.294)
Log-rank p-value		0.165

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.9 (78.3, 95.5)	80.0 (73.2, 86.8)
6 months	86.9 (78.3, 95.5)	71.5 (62.5, 80.4)
9 months	86.9 (78.3, 95.5)	69.5 (60.1, 79.0)
12 months	86.9 (78.3, 95.5)	69.5 (60.1, 79.0)
18 months	NE (NE, NE)	69.5 (60.1, 79.0)
Median Follow-up Time (months)	2.79	3.52

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	3 (4.3)	14 (9.9)
Number of Subjects Censored, n (%)	66 (95.7)	127 (90.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.215 (0.666)
95% CI		(0.600, 8.178)
Log-rank p-value		0.249

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (90.3, 100.0)	92.0 (87.5, 96.6)
6 months	95.4 (90.3, 100.0)	90.6 (85.4, 95.9)
9 months	95.4 (90.3, 100.0)	88.6 (82.1, 95.1)
12 months	95.4 (90.3, 100.0)	88.6 (82.1, 95.1)
18 months	NE (NE, NE)	88.6 (82.1, 95.1)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	0	5 (3.5)
Number of Subjects Censored, n (%)	69 (100.0)	136 (96.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.203

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.2 (93.0, 99.5)
6 months	100.0 (100.0, 100.0)	96.2 (93.0, 99.5)
9 months	100.0 (100.0, 100.0)	96.2 (93.0, 99.5)
12 months	100.0 (100.0, 100.0)	96.2 (93.0, 99.5)
18 months	NE (NE, NE)	96.2 (93.0, 99.5)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	1 (1.4)	1 (0.7)
Number of Subjects Censored, n (%)	68 (98.6)	140 (99.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.000 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.125

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.5, 100.0)	99.3 (97.8, 100.0)
6 months	98.5 (95.5, 100.0)	99.3 (97.8, 100.0)
9 months	98.5 (95.5, 100.0)	99.3 (97.8, 100.0)
12 months	98.5 (95.5, 100.0)	99.3 (97.8, 100.0)
18 months	NE (NE, NE)	99.3 (97.8, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	8 (11.6)	44 (31.2)
Number of Subjects Censored, n (%)	61 (88.4)	97 (68.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	2.76 (1.58, 5.55)
Median (95% CI)	NE (NE, NE)	13.60 (13.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.091 (0.392)
95% CI		(0.971, 4.505)
Log-rank p-value		0.069

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.0 (81.2, 96.7)	73.3 (65.8, 80.8)
6 months	82.6 (68.6, 96.6)	64.2 (54.6, 73.7)
9 months	82.6 (68.6, 96.6)	61.9 (51.6, 72.1)
12 months	82.6 (68.6, 96.6)	61.9 (51.6, 72.1)
18 months	NE (NE, NE)	41.3 (7.5, 75.0)
Median Follow-up Time (months)	2.79	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	7 (10.1)	28 (19.9)
Number of Subjects Censored, n (%)	62 (89.9)	113 (80.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	8.38 (3.75, NE)
Median (95% CI)	NE (NE, NE)	13.60 (13.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.2*, 13.0*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.292 (0.437)
95% CI		(0.549, 3.040)
Log-rank p-value		0.599

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.0 (81.2, 96.7)	83.3 (76.8, 89.7)
6 months	89.0 (81.2, 96.7)	78.4 (70.3, 86.6)
9 months	89.0 (81.2, 96.7)	72.2 (60.8, 83.5)
12 months	89.0 (81.2, 96.7)	72.2 (60.8, 83.5)
18 months	NE (NE, NE)	48.1 (8.9, 87.4)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	1 (1.4)	7 (5.0)
Number of Subjects Censored, n (%)	68 (98.6)	134 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.629 (1.085)
95% CI		(0.314, 22.035)
Log-rank p-value		0.342

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.5, 100.0)	95.6 (92.1, 99.0)
6 months	98.5 (95.5, 100.0)	94.4 (90.2, 98.5)
9 months	98.5 (95.5, 100.0)	94.4 (90.2, 98.5)
12 months	98.5 (95.5, 100.0)	94.4 (90.2, 98.5)
18 months	NE (NE, NE)	94.4 (90.2, 98.5)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	14 (20.3)	39 (27.7)
Number of Subjects Censored, n (%)	55 (79.7)	102 (72.3)
Time to first TEAE (months)		
25% percentile (95% CI)	3.71 (1.64, 5.78)	5.75 (2.53, 6.54)
Median (95% CI)	5.78 (4.34, NE)	11.53 (6.93, NE)
75% percentile (95% CI)	NE (5.78, NE)	NE (11.53, NE)
Min, Max	0.0, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.893 (0.326)
95% CI		(0.472, 1.691)
Log-rank p-value		0.795

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.9 (74.7, 93.2)	78.5 (71.3, 85.6)
6 months	30.5 (0.0, 74.6)	71.3 (62.3, 80.3)
9 months	30.5 (0.0, 74.6)	59.1 (46.6, 71.5)
12 months	30.5 (0.0, 74.6)	39.4 (6.8, 72.0)
18 months	NE (NE, NE)	39.4 (6.8, 72.0)
Median Follow-up Time (months)	2.79	3.48

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	6 (8.7)	10 (7.1)
Number of Subjects Censored, n (%)	63 (91.3)	131 (92.9)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (3.71, NE)	NE (6.93, NE)
Median (95% CI)	NE (4.14, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.327 (0.578)
95% CI		(0.106, 1.016)
Log-rank p-value		0.097

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (93.1, 100.0)	95.6 (92.1, 99.0)
6 months	68.7 (43.4, 94.0)	93.6 (88.6, 98.7)
9 months	68.7 (43.4, 94.0)	86.9 (78.1, 95.7)
12 months	68.7 (43.4, 94.0)	86.9 (78.1, 95.7)
18 months	NE (NE, NE)	86.9 (78.1, 95.7)
Median Follow-up Time (months)	2.83	4.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	2 (2.9)	7 (5.0)
Number of Subjects Censored, n (%)	67 (97.1)	134 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (11.56, NE)
Median (95% CI)	NE (NE, NE)	NE (11.56, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.870 (0.832)
95% CI		(0.170, 4.443)
Log-rank p-value		0.767

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.5, 100.0)	97.4 (94.6, 100.0)
6 months	89.5 (72.6, 100.0)	95.2 (91.0, 99.4)
9 months	89.5 (72.6, 100.0)	93.0 (87.1, 98.9)
12 months	89.5 (72.6, 100.0)	79.7 (55.1, 100.0)
18 months	NE (NE, NE)	79.7 (55.1, 100.0)
Median Follow-up Time (months)	2.83	4.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	0	1 (0.7)
Number of Subjects Censored, n (%)	69 (100.0)	140 (99.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.588

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.0 (97.0, 100.0)
6 months	100.0 (100.0, 100.0)	99.0 (97.0, 100.0)
9 months	100.0 (100.0, 100.0)	99.0 (97.0, 100.0)
12 months	100.0 (100.0, 100.0)	99.0 (97.0, 100.0)
18 months	NE (NE, NE)	99.0 (97.0, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	12 (17.4)	18 (12.8)
Number of Subjects Censored, n (%)	57 (82.6)	123 (87.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.87, NE)	NE (6.41, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.529 (0.393)
95% CI		(0.245, 1.144)
Log-rank p-value		0.169

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.0 (68.2, 89.9)	90.4 (85.4, 95.4)
6 months	79.0 (68.2, 89.9)	86.0 (79.1, 92.9)
9 months	79.0 (68.2, 89.9)	81.4 (72.4, 90.4)
12 months	79.0 (68.2, 89.9)	81.4 (72.4, 90.4)
18 months	NE (NE, NE)	81.4 (72.4, 90.4)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	10 (14.5)	10 (7.1)
Number of Subjects Censored, n (%)	59 (85.5)	131 (92.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.79, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.314 (0.484)
95% CI		(0.122, 0.811)
Log-rank p-value		0.021

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.9 (71.5, 92.3)	95.5 (91.9, 99.0)
6 months	81.9 (71.5, 92.3)	90.9 (84.6, 97.1)
9 months	81.9 (71.5, 92.3)	88.9 (81.7, 96.1)
12 months	81.9 (71.5, 92.3)	88.9 (81.7, 96.1)
18 months	NE (NE, NE)	88.9 (81.7, 96.1)
Median Follow-up Time (months)	2.79	4.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	1 (1.4)	6 (4.3)
Number of Subjects Censored, n (%)	68 (98.6)	135 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.037 (1.083)
95% CI		(0.364, 25.348)
Log-rank p-value		0.256

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.5, 100.0)	95.6 (92.2, 99.1)
6 months	98.5 (95.5, 100.0)	95.6 (92.2, 99.1)
9 months	98.5 (95.5, 100.0)	95.6 (92.2, 99.1)
12 months	98.5 (95.5, 100.0)	95.6 (92.2, 99.1)
18 months	NE (NE, NE)	95.6 (92.2, 99.1)
Median Follow-up Time (months)	2.83	4.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Endocrine disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	0	32 (22.7)
Number of Subjects Censored, n (%)	69 (100.0)	109 (77.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.68 (2.73, NE)
Median (95% CI)	NE (NE, NE)	NE (9.33, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Endocrine disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	82.5 (76.0, 89.0)
6 months	100.0 (100.0, 100.0)	72.4 (63.2, 81.6)
9 months	100.0 (100.0, 100.0)	69.9 (59.8, 80.0)
12 months	100.0 (100.0, 100.0)	63.5 (48.5, 78.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	0	31 (22.0)
Number of Subjects Censored, n (%)	69 (100.0)	110 (78.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.75 (3.65, NE)
Median (95% CI)	NE (NE, NE)	NE (9.33, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	83.2 (76.8, 89.6)
6 months	100.0 (100.0, 100.0)	74.3 (65.4, 83.3)
9 months	100.0 (100.0, 100.0)	69.1 (58.2, 80.0)
12 months	100.0 (100.0, 100.0)	62.8 (47.5, 78.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	7 (10.1)	15 (10.6)
Number of Subjects Censored, n (%)	62 (89.9)	126 (89.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.15, NE)	NE (6.74, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.810 (0.489)
95% CI		(0.311, 2.110)
Log-rank p-value		0.797

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.2 (82.7, 97.7)	92.2 (87.5, 96.9)
6 months	86.5 (76.3, 96.6)	86.7 (79.9, 93.6)
9 months	86.5 (76.3, 96.6)	84.6 (76.7, 92.4)
12 months	86.5 (76.3, 96.6)	84.6 (76.7, 92.4)
18 months	NE (NE, NE)	84.6 (76.7, 92.4)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	4 (5.8)	7 (5.0)
Number of Subjects Censored, n (%)	65 (94.2)	134 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.488 (0.677)
95% CI		(0.130, 1.840)
Log-rank p-value		0.384

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.2 (86.6, 99.7)	96.8 (93.7, 99.9)
6 months	93.2 (86.6, 99.7)	94.1 (89.3, 98.9)
9 months	93.2 (86.6, 99.7)	91.8 (85.3, 98.3)
12 months	93.2 (86.6, 99.7)	91.8 (85.3, 98.3)
18 months	NE (NE, NE)	91.8 (85.3, 98.3)
Median Follow-up Time (months)	2.83	4.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	1 (1.4)	2 (1.4)
Number of Subjects Censored, n (%)	68 (98.6)	139 (98.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.15, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.552 (1.262)
95% CI		(0.046, 6.543)
Log-rank p-value		0.705

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.2 (97.7, 100.0)
6 months	96.0 (88.3, 100.0)	97.6 (94.1, 100.0)
9 months	96.0 (88.3, 100.0)	97.6 (94.1, 100.0)
12 months	96.0 (88.3, 100.0)	97.6 (94.1, 100.0)
18 months	NE (NE, NE)	97.6 (94.1, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	1 (1.4)	2 (1.4)
Number of Subjects Censored, n (%)	68 (98.6)	139 (98.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.044 (1.228)
95% CI		(0.094, 11.586)
Log-rank p-value		0.985

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.5, 100.0)	98.4 (96.2, 100.0)
6 months	98.5 (95.5, 100.0)	98.4 (96.2, 100.0)
9 months	98.5 (95.5, 100.0)	98.4 (96.2, 100.0)
12 months	98.5 (95.5, 100.0)	98.4 (96.2, 100.0)
18 months	NE (NE, NE)	98.4 (96.2, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	9 (13.0)	11 (7.8)
Number of Subjects Censored, n (%)	60 (87.0)	130 (92.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.15, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.450 (0.454)
95% CI		(0.185, 1.096)
Log-rank p-value		0.078

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.6 (79.6, 95.7)	92.0 (87.2, 96.8)
6 months	84.0 (73.6, 94.4)	90.9 (85.7, 96.1)
9 months	84.0 (73.6, 94.4)	90.9 (85.7, 96.1)
12 months	84.0 (73.6, 94.4)	90.9 (85.7, 96.1)
18 months	NE (NE, NE)	90.9 (85.7, 96.1)
Median Follow-up Time (months)	2.83	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	1 (1.4)	5 (3.5)
Number of Subjects Censored, n (%)	68 (98.6)	136 (96.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.048 (1.099)
95% CI		(0.238, 17.659)
Log-rank p-value		0.515

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (94.7, 100.0)	95.8 (92.2, 99.4)
6 months	98.2 (94.7, 100.0)	95.8 (92.2, 99.4)
9 months	98.2 (94.7, 100.0)	95.8 (92.2, 99.4)
12 months	98.2 (94.7, 100.0)	95.8 (92.2, 99.4)
18 months	NE (NE, NE)	95.8 (92.2, 99.4)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Number of Subjects with Events, n (%)	0	3 (2.1)
Number of Subjects Censored, n (%)	69 (100.0)	138 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.222

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Rectum

Statistics	Placebo + BSC N=69	Fruquintinib + BSC N=141
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.6 (94.8, 100.0)
6 months	100.0 (100.0, 100.0)	97.6 (94.8, 100.0)
9 months	100.0 (100.0, 100.0)	97.6 (94.8, 100.0)
12 months	100.0 (100.0, 100.0)	97.6 (94.8, 100.0)
18 months	NE (NE, NE)	97.6 (94.8, 100.0)
Median Follow-up Time (months)	2.83	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	11 (47.8)	31 (79.5)
Number of Subjects Censored, n (%)	12 (52.2)	8 (20.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.76 (0.03, 1.64)	0.07 (0.07, 0.46)
Median (95% CI)	NE (0.92, NE)	0.69 (0.16, 1.12)
75% percentile (95% CI)	NE (NE, NE)	3.25 (0.95, NE)
Min, Max	0.0, 6.8*	0.0, 6.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.696 (0.369)
95% CI		(1.309, 5.555)
Log-rank p-value		0.027

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	50.8 (29.9, 71.8)	27.4 (13.1, 41.6)
6 months	50.8 (29.9, 71.8)	8.2 (0.0, 21.7)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.84	0.69

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	6 (26.1)	20 (51.3)
Number of Subjects Censored, n (%)	17 (73.9)	19 (48.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.03, NE)	0.69 (0.16, 1.61)
Median (95% CI)	NE (1.87, NE)	3.25 (0.72, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (4.70, NE)
Min, Max	0.0, 8.4*	0.1, 8.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.087 (0.490)
95% CI		(1.180, 8.072)
Log-rank p-value		0.025

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.8 (54.1, 91.5)	52.4 (36.3, 68.5)
6 months	72.8 (54.1, 91.5)	41.7 (23.1, 60.2)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.56

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	4 (17.4)	3 (7.7)
Number of Subjects Censored, n (%)	19 (82.6)	36 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.36, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 6.8*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.343 (0.795)
95% CI		(0.072, 1.630)
Log-rank p-value		0.276

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.8 (65.6, 98.0)	92.3 (83.9, 100.0)
6 months	81.8 (65.6, 98.0)	92.3 (83.9, 100.0)
9 months	NE (NE, NE)	92.3 (83.9, 100.0)
12 months	NE (NE, NE)	92.3 (83.9, 100.0)
18 months	NE (NE, NE)	92.3 (83.9, 100.0)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	1 (4.3)	5 (12.8)
Number of Subjects Censored, n (%)	22 (95.7)	34 (87.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.36, NE)	NE (3.91, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.675 (1.133)
95% CI		(0.290, 24.633)
Log-rank p-value		0.439

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	92.3 (83.9, 100.0)
6 months	95.7 (87.3, 100.0)	81.1 (64.7, 97.4)
9 months	NE (NE, NE)	81.1 (64.7, 97.4)
12 months	NE (NE, NE)	81.1 (64.7, 97.4)
18 months	NE (NE, NE)	81.1 (64.7, 97.4)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	6 (15.4)
Number of Subjects Censored, n (%)	23 (100.0)	33 (84.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.16, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.095

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	84.6 (73.3, 95.9)
6 months	100.0 (100.0, 100.0)	84.6 (73.3, 95.9)
9 months	NE (NE, NE)	84.6 (73.3, 95.9)
12 months	NE (NE, NE)	84.6 (73.3, 95.9)
18 months	NE (NE, NE)	84.6 (73.3, 95.9)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	2 (8.7)	2 (5.1)
Number of Subjects Censored, n (%)	21 (91.3)	37 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (5.95, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.549 (1.079)
95% CI		(0.066, 4.550)
Log-rank p-value		0.681

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (76.8, 100.0)	97.4 (92.3, 100.0)
6 months	90.0 (76.8, 100.0)	89.9 (75.0, 100.0)
9 months	NE (NE, NE)	89.9 (75.0, 100.0)
12 months	NE (NE, NE)	89.9 (75.0, 100.0)
18 months	NE (NE, NE)	89.9 (75.0, 100.0)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	2 (8.7)	2 (5.1)
Number of Subjects Censored, n (%)	21 (91.3)	37 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.30, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 8.4*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.936 (1.018)
95% CI		(0.127, 6.890)
Log-rank p-value		0.940

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (79.8, 100.0)	94.7 (87.4, 100.0)
6 months	91.3 (79.8, 100.0)	94.7 (87.4, 100.0)
9 months	NE (NE, NE)	94.7 (87.4, 100.0)
12 months	NE (NE, NE)	94.7 (87.4, 100.0)
18 months	NE (NE, NE)	94.7 (87.4, 100.0)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	1 (4.3)	1 (2.6)
Number of Subjects Censored, n (%)	22 (95.7)	38 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.83, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.621 (1.503)
95% CI		(0.033, 11.826)
Log-rank p-value		0.844

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.3 (80.7, 100.0)	97.2 (91.9, 100.0)
6 months	93.3 (80.7, 100.0)	97.2 (91.9, 100.0)
9 months	NE (NE, NE)	97.2 (91.9, 100.0)
12 months	NE (NE, NE)	97.2 (91.9, 100.0)
18 months	NE (NE, NE)	97.2 (91.9, 100.0)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	1 (2.6)
Number of Subjects Censored, n (%)	23 (100.0)	38 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.617

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.4 (92.5, 100.0)
6 months	100.0 (100.0, 100.0)	97.4 (92.5, 100.0)
9 months	NE (NE, NE)	97.4 (92.5, 100.0)
12 months	NE (NE, NE)	97.4 (92.5, 100.0)
18 months	NE (NE, NE)	97.4 (92.5, 100.0)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	16 (69.6)	26 (66.7)
Number of Subjects Censored, n (%)	7 (30.4)	13 (33.3)
Time to first TEAE (months)		
25% percentile (95% CI)	0.76 (0.03, 1.54)	0.49 (0.10, 0.69)
Median (95% CI)	1.61 (1.31, 2.07)	1.87 (0.69, 4.90)
75% percentile (95% CI)	NE (1.61, NE)	6.47 (2.53, NE)
Min, Max	0.0, 4.7*	0.0, 6.5
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.922 (0.335)
95% CI		(0.478, 1.779)
Log-rank p-value		0.762

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	26.7 (7.5, 45.9)	39.3 (23.6, 55.1)
6 months	NE (NE, NE)	25.3 (6.2, 44.4)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	1.58	1.31

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	3 (13.0)	8 (20.5)
Number of Subjects Censored, n (%)	20 (87.0)	31 (79.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.36, NE)	6.47 (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (6.47, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 6.8*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.462 (0.732)
95% CI		(0.348, 6.141)
Log-rank p-value		0.751

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.8 (70.9, 100.0)	84.4 (72.9, 95.9)
6 months	85.8 (70.9, 100.0)	79.1 (64.4, 93.8)
9 months	NE (NE, NE)	71.2 (51.4, 91.0)
12 months	NE (NE, NE)	71.2 (51.4, 91.0)
18 months	NE (NE, NE)	71.2 (51.4, 91.0)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	5 (21.7)	8 (20.5)
Number of Subjects Censored, n (%)	18 (78.3)	31 (79.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.16, NE)	4.07 (1.87, NE)
Median (95% CI)	NE (NE, NE)	NE (4.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.911 (0.608)
95% CI		(0.276, 3.003)
Log-rank p-value		0.764

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.7 (58.7, 94.8)	77.8 (62.5, 93.1)
6 months	76.7 (58.7, 94.8)	71.8 (53.7, 89.9)
9 months	NE (NE, NE)	71.8 (53.7, 89.9)
12 months	NE (NE, NE)	71.8 (53.7, 89.9)
18 months	NE (NE, NE)	71.8 (53.7, 89.9)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	6 (26.1)	8 (20.5)
Number of Subjects Censored, n (%)	17 (73.9)	31 (79.5)
Time to first TEAE (months)		
25% percentile (95% CI)	1.94 (0.69, NE)	12.25 (1.54, NE)
Median (95% CI)	NE (1.94, NE)	NE (12.25, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (12.25, NE)
Min, Max	0.7, 6.8*	0.7, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.518 (0.598)
95% CI		(0.160, 1.671)
Log-rank p-value		0.173

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.4 (51.9, 90.9)	81.2 (66.9, 95.5)
6 months	71.4 (51.9, 90.9)	75.4 (58.2, 92.6)
9 months	NE (NE, NE)	75.4 (58.2, 92.6)
12 months	NE (NE, NE)	75.4 (58.2, 92.6)
18 months	NE (NE, NE)	50.3 (8.4, 92.1)
Median Follow-up Time (months)	2.60	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	4 (17.4)	3 (7.7)
Number of Subjects Censored, n (%)	19 (82.6)	36 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.07, NE)	NE (2.79, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.459 (0.834)
95% CI		(0.089, 2.356)
Log-rank p-value		0.385

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.2 (62.6, 97.8)	91.2 (81.6, 100.0)
6 months	80.2 (62.6, 97.8)	91.2 (81.6, 100.0)
9 months	NE (NE, NE)	91.2 (81.6, 100.0)
12 months	NE (NE, NE)	91.2 (81.6, 100.0)
18 months	NE (NE, NE)	91.2 (81.6, 100.0)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	4 (17.4)	6 (15.4)
Number of Subjects Censored, n (%)	19 (82.6)	33 (84.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.16, NE)	7.10 (2.53, NE)
Median (95% CI)	NE (NE, NE)	NE (7.10, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.712 (0.717)
95% CI		(0.175, 2.904)
Log-rank p-value		0.424

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.9 (65.8, 98.0)	88.9 (78.7, 99.2)
6 months	81.9 (65.8, 98.0)	83.0 (68.3, 97.8)
9 months	NE (NE, NE)	69.2 (41.5, 96.8)
12 months	NE (NE, NE)	69.2 (41.5, 96.8)
18 months	NE (NE, NE)	69.2 (41.5, 96.8)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	1 (4.3)	5 (12.8)
Number of Subjects Censored, n (%)	22 (95.7)	34 (87.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	NE (0.66, NE)
Median (95% CI)	NE (NE, NE)	NE (6.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.667 (1.120)
95% CI		(0.297, 23.963)
Log-rank p-value		0.441

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	89.7 (80.2, 99.3)
6 months	95.7 (87.3, 100.0)	89.7 (80.2, 99.3)
9 months	NE (NE, NE)	76.9 (52.3, 100.0)
12 months	NE (NE, NE)	76.9 (52.3, 100.0)
18 months	NE (NE, NE)	76.9 (52.3, 100.0)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	7 (17.9)
Number of Subjects Censored, n (%)	23 (100.0)	32 (82.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.18, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.076

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	81.0 (68.3, 93.8)
6 months	100.0 (100.0, 100.0)	81.0 (68.3, 93.8)
9 months	NE (NE, NE)	81.0 (68.3, 93.8)
12 months	NE (NE, NE)	81.0 (68.3, 93.8)
18 months	NE (NE, NE)	81.0 (68.3, 93.8)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	1 (4.3)	1 (2.6)
Number of Subjects Censored, n (%)	22 (95.7)	38 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.38, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.461 (1.416)
95% CI		(0.091, 23.419)
Log-rank p-value		0.788

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (86.8, 100.0)	97.4 (92.3, 100.0)
6 months	95.5 (86.8, 100.0)	97.4 (92.3, 100.0)
9 months	NE (NE, NE)	97.4 (92.3, 100.0)
12 months	NE (NE, NE)	97.4 (92.3, 100.0)
18 months	NE (NE, NE)	97.4 (92.3, 100.0)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	1 (4.3)	0
Number of Subjects Censored, n (%)	22 (95.7)	39 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.46, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.386

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	100.0 (100.0, 100.0)
6 months	95.7 (87.3, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	1 (4.3)	0
Number of Subjects Censored, n (%)	22 (95.7)	39 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.91, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.083

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.7 (84.7, 100.0)	100.0 (100.0, 100.0)
6 months	94.7 (84.7, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	3 (7.7)
Number of Subjects Censored, n (%)	23 (100.0)	36 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.186

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	91.7 (82.8, 100.0)
6 months	100.0 (100.0, 100.0)	91.7 (82.8, 100.0)
9 months	NE (NE, NE)	91.7 (82.8, 100.0)
12 months	NE (NE, NE)	91.7 (82.8, 100.0)
18 months	NE (NE, NE)	91.7 (82.8, 100.0)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	6 (26.1)	21 (53.8)
Number of Subjects Censored, n (%)	17 (73.9)	18 (46.2)
Time to first TEAE (months)		
25% percentile (95% CI)	1.84 (0.03, NE)	0.92 (0.69, 1.64)
Median (95% CI)	NE (1.84, NE)	3.22 (1.31, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (3.94, NE)
Min, Max	0.0, 6.8*	0.1, 6.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.231 (0.478)
95% CI		(0.875, 5.688)
Log-rank p-value		0.094

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.9 (54.4, 91.5)	51.3 (34.9, 67.6)
6 months	72.9 (54.4, 91.5)	41.0 (22.8, 59.3)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.00

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	4 (17.4)	9 (23.1)
Number of Subjects Censored, n (%)	19 (82.6)	30 (76.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.608 (0.620)
95% CI		(0.477, 5.418)
Log-rank p-value		0.448

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.9 (65.8, 98.0)	75.4 (61.4, 89.5)
6 months	81.9 (65.8, 98.0)	75.4 (61.4, 89.5)
9 months	NE (NE, NE)	75.4 (61.4, 89.5)
12 months	NE (NE, NE)	75.4 (61.4, 89.5)
18 months	NE (NE, NE)	75.4 (61.4, 89.5)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	6 (15.4)
Number of Subjects Censored, n (%)	23 (100.0)	33 (84.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.64, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.108

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	86.0 (74.6, 97.4)
6 months	100.0 (100.0, 100.0)	80.3 (65.1, 95.5)
9 months	NE (NE, NE)	80.3 (65.1, 95.5)
12 months	NE (NE, NE)	80.3 (65.1, 95.5)
18 months	NE (NE, NE)	80.3 (65.1, 95.5)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	1 (4.3)	4 (10.3)
Number of Subjects Censored, n (%)	22 (95.7)	35 (89.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.72, NE)	NE (4.07, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.8*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.305 (1.149)
95% CI		(0.137, 12.408)
Log-rank p-value		0.892

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	91.9 (83.0, 100.0)
6 months	95.7 (87.3, 100.0)	85.7 (71.5, 100.0)
9 months	NE (NE, NE)	85.7 (71.5, 100.0)
12 months	NE (NE, NE)	85.7 (71.5, 100.0)
18 months	NE (NE, NE)	85.7 (71.5, 100.0)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	1 (4.3)	3 (7.7)
Number of Subjects Censored, n (%)	22 (95.7)	36 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.72, NE)	8.51 (8.51, NE)
Median (95% CI)	NE (NE, NE)	NE (8.51, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (8.51, NE)
Min, Max	0.7, 6.8*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.507 (1.258)
95% CI		(0.128, 17.750)
Log-rank p-value		0.748

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	94.9 (87.9, 100.0)
6 months	95.7 (87.3, 100.0)	94.9 (87.9, 100.0)
9 months	NE (NE, NE)	71.2 (30.6, 100.0)
12 months	NE (NE, NE)	71.2 (30.6, 100.0)
18 months	NE (NE, NE)	71.2 (30.6, 100.0)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	1 (2.6)
Number of Subjects Censored, n (%)	23 (100.0)	38 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.8, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.497

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.4 (92.5, 100.0)
6 months	100.0 (100.0, 100.0)	97.4 (92.5, 100.0)
9 months	NE (NE, NE)	97.4 (92.5, 100.0)
12 months	NE (NE, NE)	97.4 (92.5, 100.0)
18 months	NE (NE, NE)	97.4 (92.5, 100.0)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	1 (4.3)	1 (2.6)
Number of Subjects Censored, n (%)	22 (95.7)	38 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.35, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.404 (1.435)
95% CI		(0.024, 6.735)
Log-rank p-value		0.515

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (86.8, 100.0)	97.2 (91.9, 100.0)
6 months	95.5 (86.8, 100.0)	97.2 (91.9, 100.0)
9 months	NE (NE, NE)	97.2 (91.9, 100.0)
12 months	NE (NE, NE)	97.2 (91.9, 100.0)
18 months	NE (NE, NE)	97.2 (91.9, 100.0)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	5 (12.8)
Number of Subjects Censored, n (%)	23 (100.0)	34 (87.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	8.51 (3.22, NE)
Median (95% CI)	NE (NE, NE)	NE (8.51, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (8.51, NE)
Min, Max	1.3*, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.272

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (87.6, 100.0)
6 months	100.0 (100.0, 100.0)	89.8 (78.1, 100.0)
9 months	NE (NE, NE)	54.4 (9.1, 99.6)
12 months	NE (NE, NE)	54.4 (9.1, 99.6)
18 months	NE (NE, NE)	54.4 (9.1, 99.6)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	1 (2.6)
Number of Subjects Censored, n (%)	23 (100.0)	38 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.21, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	100.0 (100.0, 100.0)	94.1 (82.9, 100.0)
9 months	NE (NE, NE)	94.1 (82.9, 100.0)
12 months	NE (NE, NE)	94.1 (82.9, 100.0)
18 months	NE (NE, NE)	94.1 (82.9, 100.0)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	6 (26.1)	16 (41.0)
Number of Subjects Censored, n (%)	17 (73.9)	23 (59.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.84 (0.89, NE)	0.95 (0.69, 4.07)
Median (95% CI)	NE (1.84, NE)	16.79 (2.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (16.79, NE)
Min, Max	0.9, 6.8*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.772 (0.505)
95% CI		(0.658, 4.771)
Log-rank p-value		0.312

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.1 (53.0, 91.1)	62.3 (46.6, 78.1)
6 months	72.1 (53.0, 91.1)	56.1 (37.8, 74.4)
9 months	NE (NE, NE)	56.1 (37.8, 74.4)
12 months	NE (NE, NE)	56.1 (37.8, 74.4)
18 months	NE (NE, NE)	28.0 (0.0, 68.0)
Median Follow-up Time (months)	2.83	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	3 (13.0)	3 (7.7)
Number of Subjects Censored, n (%)	20 (87.0)	36 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.61, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.578 (0.844)
95% CI		(0.110, 3.022)
Log-rank p-value		0.477

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.0 (69.4, 100.0)	91.9 (83.0, 100.0)
6 months	85.0 (69.4, 100.0)	91.9 (83.0, 100.0)
9 months	NE (NE, NE)	91.9 (83.0, 100.0)
12 months	NE (NE, NE)	91.9 (83.0, 100.0)
18 months	NE (NE, NE)	91.9 (83.0, 100.0)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	6 (15.4)
Number of Subjects Censored, n (%)	23 (100.0)	33 (84.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.95, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.068

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	86.9 (76.1, 97.6)
6 months	100.0 (100.0, 100.0)	80.7 (65.3, 96.1)
9 months	NE (NE, NE)	80.7 (65.3, 96.1)
12 months	NE (NE, NE)	80.7 (65.3, 96.1)
18 months	NE (NE, NE)	80.7 (65.3, 96.1)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	4 (10.3)
Number of Subjects Censored, n (%)	23 (100.0)	35 (89.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.64, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.102

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	89.4 (79.6, 99.2)
6 months	100.0 (100.0, 100.0)	89.4 (79.6, 99.2)
9 months	NE (NE, NE)	89.4 (79.6, 99.2)
12 months	NE (NE, NE)	89.4 (79.6, 99.2)
18 months	NE (NE, NE)	89.4 (79.6, 99.2)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	1 (4.3)	3 (7.7)
Number of Subjects Censored, n (%)	22 (95.7)	36 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.92, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.728 (1.185)
95% CI		(0.169, 17.619)
Log-rank p-value		0.593

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	91.7 (82.6, 100.0)
6 months	95.7 (87.3, 100.0)	91.7 (82.6, 100.0)
9 months	NE (NE, NE)	91.7 (82.6, 100.0)
12 months	NE (NE, NE)	91.7 (82.6, 100.0)
18 months	NE (NE, NE)	91.7 (82.6, 100.0)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	1 (4.3)	1 (2.6)
Number of Subjects Censored, n (%)	22 (95.7)	38 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (3.71, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 6.8*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.616 (1.518)
95% CI		(0.031, 12.061)
Log-rank p-value		0.636

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.2 (91.9, 100.0)
6 months	87.5 (64.6, 100.0)	97.2 (91.9, 100.0)
9 months	NE (NE, NE)	97.2 (91.9, 100.0)
12 months	NE (NE, NE)	97.2 (91.9, 100.0)
18 months	NE (NE, NE)	97.2 (91.9, 100.0)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	2 (8.7)	4 (10.3)
Number of Subjects Censored, n (%)	21 (91.3)	35 (89.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.92, NE)	NE (4.86, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9, 6.8*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.128 (0.928)
95% CI		(0.183, 6.961)
Log-rank p-value		0.943

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (76.8, 100.0)	92.2 (83.8, 100.0)
6 months	90.0 (76.8, 100.0)	85.6 (70.9, 100.0)
9 months	NE (NE, NE)	85.6 (70.9, 100.0)
12 months	NE (NE, NE)	85.6 (70.9, 100.0)
18 months	NE (NE, NE)	85.6 (70.9, 100.0)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	4 (10.3)
Number of Subjects Censored, n (%)	23 (100.0)	35 (89.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.07, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.223

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	92.1 (83.5, 100.0)
6 months	100.0 (100.0, 100.0)	85.9 (71.8, 100.0)
9 months	NE (NE, NE)	85.9 (71.8, 100.0)
12 months	NE (NE, NE)	85.9 (71.8, 100.0)
18 months	NE (NE, NE)	85.9 (71.8, 100.0)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	1 (2.6)
Number of Subjects Censored, n (%)	23 (100.0)	38 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.248

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.4 (92.5, 100.0)
6 months	100.0 (100.0, 100.0)	97.4 (92.5, 100.0)
9 months	NE (NE, NE)	97.4 (92.5, 100.0)
12 months	NE (NE, NE)	97.4 (92.5, 100.0)
18 months	NE (NE, NE)	97.4 (92.5, 100.0)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	1 (2.6)
Number of Subjects Censored, n (%)	23 (100.0)	38 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.99, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.593

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.0 (85.4, 100.0)
6 months	100.0 (100.0, 100.0)	95.0 (85.4, 100.0)
9 months	NE (NE, NE)	95.0 (85.4, 100.0)
12 months	NE (NE, NE)	95.0 (85.4, 100.0)
18 months	NE (NE, NE)	95.0 (85.4, 100.0)
Median Follow-up Time (months)	2.83	2.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	6 (26.1)	16 (41.0)
Number of Subjects Censored, n (%)	17 (73.9)	23 (59.0)
Time to first TEAE (months)		
25% percentile (95% CI)	2.76 (0.36, NE)	0.16 (0.03, 2.73)
Median (95% CI)	NE (2.76, NE)	NE (0.92, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 8.4*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.766 (0.492)
95% CI		(0.674, 4.631)
Log-rank p-value		0.328

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	70.6 (50.4, 90.7)	61.0 (45.4, 76.5)
6 months	70.6 (50.4, 90.7)	55.4 (37.9, 72.9)
9 months	NE (NE, NE)	55.4 (37.9, 72.9)
12 months	NE (NE, NE)	55.4 (37.9, 72.9)
18 months	NE (NE, NE)	55.4 (37.9, 72.9)
Median Follow-up Time (months)	2.83	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	6 (15.4)
Number of Subjects Censored, n (%)	23 (100.0)	33 (84.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.16, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.079

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	84.6 (73.3, 95.9)
6 months	100.0 (100.0, 100.0)	84.6 (73.3, 95.9)
9 months	NE (NE, NE)	84.6 (73.3, 95.9)
12 months	NE (NE, NE)	84.6 (73.3, 95.9)
18 months	NE (NE, NE)	84.6 (73.3, 95.9)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	4 (17.4)	7 (17.9)
Number of Subjects Censored, n (%)	19 (82.6)	32 (82.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.36, NE)	NE (0.82, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.100 (0.646)
95% CI		(0.310, 3.903)
Log-rank p-value		0.882

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.1 (64.2, 97.9)	81.6 (69.2, 94.0)
6 months	81.1 (64.2, 97.9)	81.6 (69.2, 94.0)
9 months	NE (NE, NE)	81.6 (69.2, 94.0)
12 months	NE (NE, NE)	81.6 (69.2, 94.0)
18 months	NE (NE, NE)	81.6 (69.2, 94.0)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	3 (13.0)	3 (7.7)
Number of Subjects Censored, n (%)	20 (87.0)	36 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.36, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.553 (0.858)
95% CI		(0.103, 2.972)
Log-rank p-value		0.488

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.7 (72.7, 100.0)	91.7 (82.7, 100.0)
6 months	86.7 (72.7, 100.0)	91.7 (82.7, 100.0)
9 months	NE (NE, NE)	91.7 (82.7, 100.0)
12 months	NE (NE, NE)	91.7 (82.7, 100.0)
18 months	NE (NE, NE)	91.7 (82.7, 100.0)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	1 (2.6)
Number of Subjects Censored, n (%)	23 (100.0)	38 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.450

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.3 (92.1, 100.0)
6 months	100.0 (100.0, 100.0)	97.3 (92.1, 100.0)
9 months	NE (NE, NE)	97.3 (92.1, 100.0)
12 months	NE (NE, NE)	97.3 (92.1, 100.0)
18 months	NE (NE, NE)	97.3 (92.1, 100.0)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	1 (2.6)
Number of Subjects Censored, n (%)	23 (100.0)	38 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.80, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	100.0 (100.0, 100.0)	93.8 (81.9, 100.0)
9 months	NE (NE, NE)	93.8 (81.9, 100.0)
12 months	NE (NE, NE)	93.8 (81.9, 100.0)
18 months	NE (NE, NE)	93.8 (81.9, 100.0)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Vascular disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	5 (21.7)	24 (61.5)
Number of Subjects Censored, n (%)	18 (78.3)	15 (38.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	0.69 (0.07, 0.69)
Median (95% CI)	NE (NE, NE)	1.58 (0.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (2.14, NE)
Min, Max	0.6, 8.4*	0.1, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.384 (0.511)
95% CI		(1.611, 11.928)
Log-rank p-value		0.004

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Vascular disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.1 (57.5, 94.7)	36.6 (21.0, 52.3)
6 months	76.1 (57.5, 94.7)	36.6 (21.0, 52.3)
9 months	NE (NE, NE)	36.6 (21.0, 52.3)
12 months	NE (NE, NE)	36.6 (21.0, 52.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	0.89

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	3 (13.0)	24 (61.5)
Number of Subjects Censored, n (%)	20 (87.0)	15 (38.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	0.69 (0.07, 0.69)
Median (95% CI)	NE (NE, NE)	1.58 (0.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (2.14, NE)
Min, Max	0.6, 8.4*	0.1, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		7.523 (0.631)
95% CI		(2.183, 25.928)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.6 (68.3, 100.0)	36.6 (21.0, 52.3)
6 months	84.6 (68.3, 100.0)	36.6 (21.0, 52.3)
9 months	NE (NE, NE)	36.6 (21.0, 52.3)
12 months	NE (NE, NE)	36.6 (21.0, 52.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	0.89

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	5 (21.7)	13 (33.3)
Number of Subjects Censored, n (%)	18 (78.3)	26 (66.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	2.99 (0.76, 5.29)
Median (95% CI)	NE (NE, NE)	NE (4.70, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.633 (0.564)
95% CI		(0.540, 4.932)
Log-rank p-value		0.522

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.3 (61.4, 95.1)	72.3 (57.3, 87.4)
6 months	78.3 (61.4, 95.1)	56.0 (35.9, 76.0)
9 months	NE (NE, NE)	56.0 (35.9, 76.0)
12 months	NE (NE, NE)	56.0 (35.9, 76.0)
18 months	NE (NE, NE)	56.0 (35.9, 76.0)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	2 (8.7)	8 (20.5)
Number of Subjects Censored, n (%)	21 (91.3)	31 (79.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	4.70 (0.79, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.957 (0.843)
95% CI		(0.567, 15.421)
Log-rank p-value		0.281

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (79.8, 100.0)	79.4 (65.1, 93.6)
6 months	91.3 (79.8, 100.0)	73.7 (56.7, 90.7)
9 months	NE (NE, NE)	73.7 (56.7, 90.7)
12 months	NE (NE, NE)	73.7 (56.7, 90.7)
18 months	NE (NE, NE)	73.7 (56.7, 90.7)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	1 (4.3)	3 (7.7)
Number of Subjects Censored, n (%)	22 (95.7)	36 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.91, NE)	NE (5.16, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.118 (1.178)
95% CI		(0.111, 11.250)
Log-rank p-value		1.000

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.7 (84.7, 100.0)	94.7 (87.4, 100.0)
6 months	94.7 (84.7, 100.0)	87.4 (72.1, 100.0)
9 months	NE (NE, NE)	87.4 (72.1, 100.0)
12 months	NE (NE, NE)	87.4 (72.1, 100.0)
18 months	NE (NE, NE)	87.4 (72.1, 100.0)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	2 (8.7)	1 (2.6)
Number of Subjects Censored, n (%)	21 (91.3)	38 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.16, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.9, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.455 (1.256)
95% CI		(0.039, 5.328)
Log-rank p-value		0.606

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (79.8, 100.0)	97.4 (92.5, 100.0)
6 months	91.3 (79.8, 100.0)	97.4 (92.5, 100.0)
9 months	NE (NE, NE)	97.4 (92.5, 100.0)
12 months	NE (NE, NE)	97.4 (92.5, 100.0)
18 months	NE (NE, NE)	97.4 (92.5, 100.0)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	1 (2.6)
Number of Subjects Censored, n (%)	23 (100.0)	38 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.280

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.2 (91.9, 100.0)
6 months	100.0 (100.0, 100.0)	97.2 (91.9, 100.0)
9 months	NE (NE, NE)	97.2 (91.9, 100.0)
12 months	NE (NE, NE)	97.2 (91.9, 100.0)
18 months	NE (NE, NE)	97.2 (91.9, 100.0)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	1 (2.6)
Number of Subjects Censored, n (%)	23 (100.0)	38 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.8, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.248

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.4 (92.5, 100.0)
6 months	100.0 (100.0, 100.0)	97.4 (92.5, 100.0)
9 months	NE (NE, NE)	97.4 (92.5, 100.0)
12 months	NE (NE, NE)	97.4 (92.5, 100.0)
18 months	NE (NE, NE)	97.4 (92.5, 100.0)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	2 (8.7)	12 (30.8)
Number of Subjects Censored, n (%)	21 (91.3)	27 (69.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.54, NE)	1.61 (0.53, NE)
Median (95% CI)	NE (3.71, NE)	NE (3.58, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.427 (0.784)
95% CI		(0.738, 15.920)
Log-rank p-value		0.187

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.2 (86.1, 100.0)	74.1 (60.2, 87.9)
6 months	81.6 (55.7, 100.0)	62.2 (43.0, 81.3)
9 months	NE (NE, NE)	62.2 (43.0, 81.3)
12 months	NE (NE, NE)	62.2 (43.0, 81.3)
18 months	NE (NE, NE)	62.2 (43.0, 81.3)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	8 (20.5)
Number of Subjects Censored, n (%)	23 (100.0)	31 (79.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.11 (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (4.11, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.087

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	84.6 (73.3, 95.9)
6 months	100.0 (100.0, 100.0)	72.0 (53.2, 90.8)
9 months	NE (NE, NE)	72.0 (53.2, 90.8)
12 months	NE (NE, NE)	72.0 (53.2, 90.8)
18 months	NE (NE, NE)	72.0 (53.2, 90.8)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	1 (4.3)	0
Number of Subjects Censored, n (%)	22 (95.7)	39 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (3.71, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.083

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	87.5 (64.6, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	3 (13.0)	7 (17.9)
Number of Subjects Censored, n (%)	20 (87.0)	32 (82.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.07, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.523 (0.714)
95% CI		(0.376, 6.172)
Log-rank p-value		0.656

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.2 (69.5, 100.0)	81.8 (69.6, 94.0)
6 months	85.2 (69.5, 100.0)	81.8 (69.6, 94.0)
9 months	NE (NE, NE)	81.8 (69.6, 94.0)
12 months	NE (NE, NE)	81.8 (69.6, 94.0)
18 months	NE (NE, NE)	81.8 (69.6, 94.0)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	2 (8.7)	2 (5.1)
Number of Subjects Censored, n (%)	21 (91.3)	37 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.07, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.721 (1.034)
95% CI		(0.095, 5.465)
Log-rank p-value		0.756

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (79.8, 100.0)	94.8 (87.8, 100.0)
6 months	91.3 (79.8, 100.0)	94.8 (87.8, 100.0)
9 months	NE (NE, NE)	94.8 (87.8, 100.0)
12 months	NE (NE, NE)	94.8 (87.8, 100.0)
18 months	NE (NE, NE)	94.8 (87.8, 100.0)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	1 (2.6)
Number of Subjects Censored, n (%)	23 (100.0)	38 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.497

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.3 (92.1, 100.0)
6 months	100.0 (100.0, 100.0)	97.3 (92.1, 100.0)
9 months	NE (NE, NE)	97.3 (92.1, 100.0)
12 months	NE (NE, NE)	97.3 (92.1, 100.0)
18 months	NE (NE, NE)	97.3 (92.1, 100.0)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	6 (26.1)	10 (25.6)
Number of Subjects Censored, n (%)	17 (73.9)	29 (74.4)
Time to first TEAE (months)		
25% percentile (95% CI)	1.77 (0.79, NE)	2.69 (0.69, NE)
Median (95% CI)	NE (1.77, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8, 8.4*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.152 (0.534)
95% CI		(0.405, 3.277)
Log-rank p-value		0.715

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.9 (52.7, 91.1)	72.6 (58.0, 87.2)
6 months	71.9 (52.7, 91.1)	72.6 (58.0, 87.2)
9 months	NE (NE, NE)	72.6 (58.0, 87.2)
12 months	NE (NE, NE)	72.6 (58.0, 87.2)
18 months	NE (NE, NE)	72.6 (58.0, 87.2)
Median Follow-up Time (months)	2.79	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	1 (4.3)	8 (20.5)
Number of Subjects Censored, n (%)	22 (95.7)	31 (79.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.82, NE)	NE (0.92, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8, 8.4*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.318 (1.064)
95% CI		(0.537, 34.734)
Log-rank p-value		0.134

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	77.6 (63.7, 91.4)
6 months	95.7 (87.3, 100.0)	77.6 (63.7, 91.4)
9 months	NE (NE, NE)	77.6 (63.7, 91.4)
12 months	NE (NE, NE)	77.6 (63.7, 91.4)
18 months	NE (NE, NE)	77.6 (63.7, 91.4)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	1 (2.6)
Number of Subjects Censored, n (%)	23 (100.0)	38 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.248

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.4 (92.3, 100.0)
6 months	100.0 (100.0, 100.0)	97.4 (92.3, 100.0)
9 months	NE (NE, NE)	97.4 (92.3, 100.0)
12 months	NE (NE, NE)	97.4 (92.3, 100.0)
18 months	NE (NE, NE)	97.4 (92.3, 100.0)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	5 (21.7)	6 (15.4)
Number of Subjects Censored, n (%)	18 (78.3)	33 (84.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.13, NE)	17.48 (1.91, NE)
Median (95% CI)	NE (NE, NE)	17.48 (6.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.48, NE)
Min, Max	0.1, 6.8*	0.5, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.543 (0.694)
95% CI		(0.139, 2.117)
Log-rank p-value		0.431

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.3 (61.4, 95.1)	89.5 (79.8, 99.3)
6 months	78.3 (61.4, 95.1)	89.5 (79.8, 99.3)
9 months	NE (NE, NE)	76.7 (52.1, 100.0)
12 months	NE (NE, NE)	76.7 (52.1, 100.0)
18 months	NE (NE, NE)	38.4 (0.0, 92.9)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	2 (5.1)
Number of Subjects Censored, n (%)	23 (100.0)	37 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.327

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.8 (87.8, 100.0)
6 months	100.0 (100.0, 100.0)	94.8 (87.8, 100.0)
9 months	NE (NE, NE)	94.8 (87.8, 100.0)
12 months	NE (NE, NE)	94.8 (87.8, 100.0)
18 months	NE (NE, NE)	94.8 (87.8, 100.0)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	1 (4.3)	0
Number of Subjects Censored, n (%)	22 (95.7)	39 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.386

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	100.0 (100.0, 100.0)
6 months	95.7 (87.3, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	1 (4.3)	1 (2.6)
Number of Subjects Censored, n (%)	22 (95.7)	38 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.43, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 8.4*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.433 (1.418)
95% CI		(0.027, 6.973)
Log-rank p-value		0.544

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	97.4 (92.5, 100.0)
6 months	95.7 (87.3, 100.0)	97.4 (92.5, 100.0)
9 months	NE (NE, NE)	97.4 (92.5, 100.0)
12 months	NE (NE, NE)	97.4 (92.5, 100.0)
18 months	NE (NE, NE)	97.4 (92.5, 100.0)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	5 (21.7)	13 (33.3)
Number of Subjects Censored, n (%)	18 (78.3)	26 (66.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	0.69 (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (2.27, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 8.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.741 (0.539)
95% CI		(0.605, 5.006)
Log-rank p-value		0.315

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.5 (60.1, 94.9)	65.3 (49.9, 80.7)
6 months	77.5 (60.1, 94.9)	65.3 (49.9, 80.7)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	5 (21.7)	8 (20.5)
Number of Subjects Censored, n (%)	18 (78.3)	31 (79.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	17.74 (0.92, NE)
Median (95% CI)	NE (NE, NE)	17.74 (17.74, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.74, NE)
Min, Max	0.0, 6.8*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.806 (0.606)
95% CI		(0.246, 2.645)
Log-rank p-value		0.803

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.5 (60.1, 94.9)	80.7 (67.7, 93.6)
6 months	77.5 (60.1, 94.9)	80.7 (67.7, 93.6)
9 months	NE (NE, NE)	80.7 (67.7, 93.6)
12 months	NE (NE, NE)	80.7 (67.7, 93.6)
18 months	NE (NE, NE)	40.3 (0.0, 96.6)
Median Follow-up Time (months)	2.79	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	7 (17.9)
Number of Subjects Censored, n (%)	23 (100.0)	32 (82.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.7, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.050

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	82.1 (70.0, 94.1)
6 months	100.0 (100.0, 100.0)	82.1 (70.0, 94.1)
9 months	NE (NE, NE)	82.1 (70.0, 94.1)
12 months	NE (NE, NE)	82.1 (70.0, 94.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Endocrine disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	11 (28.2)
Number of Subjects Censored, n (%)	23 (100.0)	28 (71.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.81 (1.15, 6.01)
Median (95% CI)	NE (NE, NE)	6.01 (4.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (6.01, NE)
Min, Max	1.3*, 8.4*	0.7, 12.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.037

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Endocrine disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	80.6 (67.5, 93.6)
6 months	100.0 (100.0, 100.0)	58.6 (35.4, 81.8)
9 months	NE (NE, NE)	48.8 (22.7, 74.9)
12 months	NE (NE, NE)	48.8 (22.7, 74.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	11 (28.2)
Number of Subjects Censored, n (%)	23 (100.0)	28 (71.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.81 (1.15, 6.01)
Median (95% CI)	NE (NE, NE)	6.01 (4.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (6.01, NE)
Min, Max	1.3*, 8.4*	0.7, 12.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.037

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	80.6 (67.5, 93.6)
6 months	100.0 (100.0, 100.0)	58.6 (35.4, 81.8)
9 months	NE (NE, NE)	48.8 (22.7, 74.9)
12 months	NE (NE, NE)	48.8 (22.7, 74.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	2 (8.7)	3 (7.7)
Number of Subjects Censored, n (%)	21 (91.3)	36 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	NE (2.99, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.556 (1.025)
95% CI		(0.075, 4.149)
Log-rank p-value		0.693

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (79.8, 100.0)	89.7 (78.1, 100.0)
6 months	91.3 (79.8, 100.0)	89.7 (78.1, 100.0)
9 months	NE (NE, NE)	89.7 (78.1, 100.0)
12 months	NE (NE, NE)	89.7 (78.1, 100.0)
18 months	NE (NE, NE)	89.7 (78.1, 100.0)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	2 (8.7)	1 (2.6)
Number of Subjects Censored, n (%)	21 (91.3)	38 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.306 (1.254)
95% CI		(0.026, 3.570)
Log-rank p-value		0.346

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (79.8, 100.0)	97.4 (92.5, 100.0)
6 months	91.3 (79.8, 100.0)	97.4 (92.5, 100.0)
9 months	NE (NE, NE)	97.4 (92.5, 100.0)
12 months	NE (NE, NE)	97.4 (92.5, 100.0)
18 months	NE (NE, NE)	97.4 (92.5, 100.0)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	1 (2.6)
Number of Subjects Censored, n (%)	23 (100.0)	38 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.99, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.0 (85.4, 100.0)
6 months	100.0 (100.0, 100.0)	95.0 (85.4, 100.0)
9 months	NE (NE, NE)	95.0 (85.4, 100.0)
12 months	NE (NE, NE)	95.0 (85.4, 100.0)
18 months	NE (NE, NE)	95.0 (85.4, 100.0)
Median Follow-up Time (months)	2.83	2.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	2 (8.7)	7 (17.9)
Number of Subjects Censored, n (%)	21 (91.3)	32 (82.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.30, NE)	9.66 (1.87, NE)
Median (95% CI)	NE (NE, NE)	NE (9.66, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (9.66, NE)
Min, Max	0.3, 8.4*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.670 (0.869)
95% CI		(0.304, 9.178)
Log-rank p-value		0.607

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.1 (79.3, 100.0)	86.5 (75.4, 97.5)
6 months	91.1 (79.3, 100.0)	81.4 (67.2, 95.6)
9 months	NE (NE, NE)	81.4 (67.2, 95.6)
12 months	NE (NE, NE)	61.0 (24.9, 97.2)
18 months	NE (NE, NE)	61.0 (24.9, 97.2)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	2 (5.1)
Number of Subjects Censored, n (%)	23 (100.0)	37 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	9.66 (9.66, NE)
Median (95% CI)	NE (NE, NE)	NE (9.66, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (9.66, NE)
Min, Max	1.3*, 8.4*	0.9*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.564

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.2 (91.9, 100.0)
6 months	100.0 (100.0, 100.0)	97.2 (91.9, 100.0)
9 months	NE (NE, NE)	97.2 (91.9, 100.0)
12 months	NE (NE, NE)	72.9 (31.5, 100.0)
18 months	NE (NE, NE)	72.9 (31.5, 100.0)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3G
Summary of Time to Onset of TEAE by SOC/PT by Primary Tumor Site at 1st Diagnosis
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Colon and Rectum

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Number of Subjects with Events, n (%)	0	2 (5.1)
Number of Subjects Censored, n (%)	23 (100.0)	37 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.3*, 8.4*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.196

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
WT (Wild Type)

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=39
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (87.4, 100.0)
6 months	100.0 (100.0, 100.0)	94.7 (87.4, 100.0)
9 months	NE (NE, NE)	94.7 (87.4, 100.0)
12 months	NE (NE, NE)	94.7 (87.4, 100.0)
18 months	NE (NE, NE)	94.7 (87.4, 100.0)
Median Follow-up Time (months)	2.83	3.02

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	55 (64.7)	121 (71.6)
Number of Subjects Censored, n (%)	30 (35.3)	48 (28.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.49 (0.16, 0.72)	0.26 (0.16, 0.46)
Median (95% CI)	1.58 (0.92, 2.60)	0.95 (0.69, 1.84)
75% percentile (95% CI)	4.70 (3.19, NE)	5.59 (3.71, 7.39)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Min, Max	0.0, 6.8*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.035 (0.165)
95% CI		(0.749, 1.431)
Log-rank p-value		0.852

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	36.7 (26.1, 47.3)	38.4 (31.0, 45.9)
6 months	24.4 (10.1, 38.7)	24.6 (16.7, 32.5)
9 months	NE (NE, NE)	13.8 (5.3, 22.2)
12 months	NE (NE, NE)	13.8 (5.3, 22.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.35	0.95

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	24 (28.2)	63 (37.3)
Number of Subjects Censored, n (%)	61 (71.8)	106 (62.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.72, NE)	0.99 (0.69, 1.87)
Median (95% CI)	NE (4.70, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.218 (0.242)
95% CI		(0.758, 1.959)
Log-rank p-value		0.435

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.6 (61.6, 81.5)	64.1 (56.7, 71.5)
6 months	62.6 (44.1, 81.2)	60.9 (53.0, 68.8)
9 months	NE (NE, NE)	59.1 (50.8, 67.5)
12 months	NE (NE, NE)	59.1 (50.8, 67.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	15 (17.6)	36 (21.3)
Number of Subjects Censored, n (%)	70 (82.4)	133 (78.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.58, NE)	6.97 (2.76, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.064 (0.312)
95% CI		(0.578, 1.960)
Log-rank p-value		0.892

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.1 (72.4, 89.8)	81.8 (75.9, 87.7)
6 months	81.1 (72.4, 89.8)	77.5 (70.5, 84.5)
9 months	NE (NE, NE)	72.3 (62.8, 81.8)
12 months	NE (NE, NE)	72.3 (62.8, 81.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.09

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	10 (11.8)	24 (14.2)
Number of Subjects Censored, n (%)	75 (88.2)	145 (85.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.70, NE)	NE (6.41, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.022 (0.382)
95% CI		(0.483, 2.163)
Log-rank p-value		0.974

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.4 (81.2, 95.6)	88.4 (83.5, 93.3)
6 months	79.6 (61.9, 97.2)	84.3 (78.2, 90.4)
9 months	NE (NE, NE)	82.5 (75.6, 89.5)
12 months	NE (NE, NE)	82.5 (75.6, 89.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	1 (1.2)	20 (11.8)
Number of Subjects Censored, n (%)	84 (98.8)	149 (88.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.26, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		8.411 (1.028)
95% CI		(1.121, 63.106)
Log-rank p-value		0.013

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.5, 100.0)	89.7 (85.0, 94.3)
6 months	98.8 (96.5, 100.0)	87.6 (82.3, 93.0)
9 months	NE (NE, NE)	84.4 (76.3, 92.5)
12 months	NE (NE, NE)	84.4 (76.3, 92.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	11 (12.9)	9 (5.3)
Number of Subjects Censored, n (%)	74 (87.1)	160 (94.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.19, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.259 (0.473)
95% CI		(0.103, 0.655)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (79.7, 95.2)	96.1 (93.1, 99.2)
6 months	79.5 (66.6, 92.3)	92.6 (87.7, 97.5)
9 months	NE (NE, NE)	92.6 (87.7, 97.5)
12 months	NE (NE, NE)	92.6 (87.7, 97.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	5 (5.9)	6 (3.6)
Number of Subjects Censored, n (%)	80 (94.1)	163 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.97, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.374 (0.672)
95% CI		(0.100, 1.395)
Log-rank p-value		0.119

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.0 (88.8, 99.1)	96.8 (94.1, 99.6)
6 months	94.0 (88.8, 99.1)	96.8 (94.1, 99.6)
9 months	NE (NE, NE)	91.5 (80.9, 100.0)
12 months	NE (NE, NE)	91.5 (80.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	2 (2.4)	9 (5.3)
Number of Subjects Censored, n (%)	83 (97.6)	160 (94.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.00, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.3, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.076 (0.835)
95% CI		(0.210, 5.528)
Log-rank p-value		0.959

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (93.5, 100.0)	98.2 (96.2, 100.0)
6 months	97.3 (93.5, 100.0)	94.7 (90.4, 99.1)
9 months	NE (NE, NE)	91.6 (84.2, 99.0)
12 months	NE (NE, NE)	78.4 (59.9, 96.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	1 (1.2)	6 (3.6)
Number of Subjects Censored, n (%)	84 (98.8)	163 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.694 (1.120)
95% CI		(0.189, 15.215)
Log-rank p-value		0.702

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.9 (93.7, 100.0)	96.7 (93.8, 99.6)
6 months	97.9 (93.7, 100.0)	96.7 (93.8, 99.6)
9 months	NE (NE, NE)	93.3 (86.3, 100.0)
12 months	NE (NE, NE)	93.3 (86.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	0	4 (2.4)
Number of Subjects Censored, n (%)	85 (100.0)	165 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.179

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.2 (96.2, 100.0)
6 months	100.0 (100.0, 100.0)	97.2 (94.4, 100.0)
9 months	NE (NE, NE)	97.2 (94.4, 100.0)
12 months	NE (NE, NE)	97.2 (94.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	56 (65.9)	113 (66.9)
Number of Subjects Censored, n (%)	29 (34.1)	56 (33.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.36 (0.07, 0.66)	0.49 (0.26, 0.69)
Median (95% CI)	1.31 (0.69, 1.84)	1.64 (0.95, 2.37)
75% percentile (95% CI)	3.75 (2.07, NE)	7.75 (3.75, NE)
Min, Max	0.0, 5.6*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.865 (0.166)
95% CI		(0.625, 1.198)
Log-rank p-value		0.355

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	32.1 (20.9, 43.2)	37.8 (30.2, 45.4)
6 months	NE (NE, NE)	27.2 (18.9, 35.5)
9 months	NE (NE, NE)	20.4 (10.1, 30.7)
12 months	NE (NE, NE)	20.4 (10.1, 30.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.08	1.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	8 (9.4)	42 (24.9)
Number of Subjects Censored, n (%)	77 (90.6)	127 (75.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.39 (1.91, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.381 (0.389)
95% CI		(1.110, 5.105)
Log-rank p-value		0.023

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.4 (84.0, 96.7)	78.5 (72.2, 84.8)
6 months	90.4 (84.0, 96.7)	70.3 (61.3, 79.3)
9 months	NE (NE, NE)	66.2 (56.1, 76.3)
12 months	NE (NE, NE)	66.2 (56.1, 76.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	18 (21.2)	32 (18.9)
Number of Subjects Censored, n (%)	67 (78.8)	137 (81.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.76, NE)	9.00 (3.94, NE)
Median (95% CI)	NE (NE, NE)	NE (9.20, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.688 (0.303)
95% CI		(0.380, 1.245)
Log-rank p-value		0.222

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.1 (69.1, 87.1)	83.5 (77.7, 89.4)
6 months	78.1 (69.1, 87.1)	80.3 (73.6, 87.0)
9 months	NE (NE, NE)	78.3 (70.8, 85.9)
12 months	NE (NE, NE)	67.5 (52.1, 82.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	17 (20.0)	29 (17.2)
Number of Subjects Censored, n (%)	68 (80.0)	140 (82.8)
Time to first TEAE (months)		
25% percentile (95% CI)	4.57 (1.45, NE)	7.98 (6.41, NE)
Median (95% CI)	NE (4.57, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.649 (0.316)
95% CI		(0.350, 1.206)
Log-rank p-value		0.163

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.4 (68.4, 88.3)	86.9 (81.7, 92.2)
6 months	70.5 (53.4, 87.6)	82.9 (76.6, 89.2)
9 months	NE (NE, NE)	74.5 (63.7, 85.4)
12 months	NE (NE, NE)	68.3 (53.0, 83.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.52

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	14 (16.5)	31 (18.3)
Number of Subjects Censored, n (%)	71 (83.5)	138 (81.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.07, NE)	NE (3.75, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.909 (0.327)
95% CI		(0.479, 1.723)
Log-rank p-value		0.716

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.6 (71.8, 91.4)	83.6 (77.8, 89.4)
6 months	78.2 (66.8, 89.7)	77.3 (69.6, 85.0)
9 months	NE (NE, NE)	77.3 (69.6, 85.0)
12 months	NE (NE, NE)	77.3 (69.6, 85.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	10 (11.8)	27 (16.0)
Number of Subjects Censored, n (%)	75 (88.2)	142 (84.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.52, NE)	9.20 (6.47, NE)
Median (95% CI)	NE (NE, NE)	NE (10.18, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.025 (0.381)
95% CI		(0.485, 2.163)
Log-rank p-value		0.956

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.4 (81.3, 95.6)	87.6 (82.5, 92.7)
6 months	83.8 (72.6, 94.9)	84.1 (77.8, 90.4)
9 months	NE (NE, NE)	79.7 (71.1, 88.2)
12 months	NE (NE, NE)	65.4 (45.8, 84.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	7 (8.2)	28 (16.6)
Number of Subjects Censored, n (%)	78 (91.8)	141 (83.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.98, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.028 (0.426)
95% CI		(0.880, 4.673)
Log-rank p-value		0.079

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.2 (84.9, 97.4)	85.0 (79.6, 90.5)
6 months	91.2 (84.9, 97.4)	82.8 (76.7, 88.9)
9 months	NE (NE, NE)	79.5 (70.9, 88.2)
12 months	NE (NE, NE)	79.5 (70.9, 88.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	2 (2.4)	11 (6.5)
Number of Subjects Censored, n (%)	83 (97.6)	158 (93.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.399 (0.777)
95% CI		(0.523, 11.010)
Log-rank p-value		0.269

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (93.9, 100.0)	94.4 (90.9, 98.0)
6 months	97.4 (93.9, 100.0)	93.4 (89.3, 97.4)
9 months	NE (NE, NE)	90.1 (82.8, 97.5)
12 months	NE (NE, NE)	90.1 (82.8, 97.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	2 (2.4)	6 (3.6)
Number of Subjects Censored, n (%)	83 (97.6)	163 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.507 (0.817)
95% CI		(0.304, 7.475)
Log-rank p-value		0.634

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (93.9, 100.0)	96.4 (93.6, 99.2)
6 months	97.4 (93.9, 100.0)	96.4 (93.6, 99.2)
9 months	NE (NE, NE)	96.4 (93.6, 99.2)
12 months	NE (NE, NE)	96.4 (93.6, 99.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	1 (1.2)	4 (2.4)
Number of Subjects Censored, n (%)	84 (98.8)	165 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.779 (1.121)
95% CI		(0.198, 15.993)
Log-rank p-value		0.559

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.4, 100.0)	97.4 (94.8, 100.0)
6 months	98.8 (96.4, 100.0)	97.4 (94.8, 100.0)
9 months	NE (NE, NE)	97.4 (94.8, 100.0)
12 months	NE (NE, NE)	97.4 (94.8, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	5 (5.9)	1 (0.6)
Number of Subjects Censored, n (%)	80 (94.1)	168 (99.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.091 (1.096)
95% CI		(0.011, 0.778)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.4 (87.7, 99.0)	99.4 (98.2, 100.0)
6 months	93.4 (87.7, 99.0)	99.4 (98.2, 100.0)
9 months	NE (NE, NE)	99.4 (98.2, 100.0)
12 months	NE (NE, NE)	99.4 (98.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	0	8 (4.7)
Number of Subjects Censored, n (%)	85 (100.0)	161 (95.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.045

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.0 (91.5, 98.4)
6 months	100.0 (100.0, 100.0)	95.0 (91.5, 98.4)
9 months	NE (NE, NE)	95.0 (91.5, 98.4)
12 months	NE (NE, NE)	95.0 (91.5, 98.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	27 (31.8)	70 (41.4)
Number of Subjects Censored, n (%)	58 (68.2)	99 (58.6)
Time to first TEAE (months)		
25% percentile (95% CI)	1.25 (0.69, NE)	1.48 (0.89, 1.87)
Median (95% CI)	NE (NE, NE)	NE (4.63, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.145 (0.229)
95% CI		(0.731, 1.794)
Log-rank p-value		0.666

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	68.4 (58.3, 78.5)	62.8 (55.3, 70.3)
6 months	65.0 (53.4, 76.6)	55.5 (47.0, 63.9)
9 months	NE (NE, NE)	50.9 (40.9, 60.9)
12 months	NE (NE, NE)	50.9 (40.9, 60.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.46	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	20 (23.5)	48 (28.4)
Number of Subjects Censored, n (%)	65 (76.5)	121 (71.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.76, NE)	2.92 (1.61, 6.97)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.059 (0.269)
95% CI		(0.625, 1.794)
Log-rank p-value		0.920

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.8 (66.6, 85.1)	73.7 (66.8, 80.6)
6 months	75.8 (66.6, 85.1)	68.6 (60.8, 76.4)
9 months	NE (NE, NE)	66.4 (57.7, 75.0)
12 months	NE (NE, NE)	66.4 (57.7, 75.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	1 (1.2)	7 (4.1)
Number of Subjects Censored, n (%)	84 (98.8)	162 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.596 (1.083)
95% CI		(0.311, 21.678)
Log-rank p-value		0.333

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.4, 100.0)	96.0 (92.9, 99.2)
6 months	98.8 (96.4, 100.0)	96.0 (92.9, 99.2)
9 months	NE (NE, NE)	92.8 (85.9, 99.7)
12 months	NE (NE, NE)	92.8 (85.9, 99.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	3 (3.5)	5 (3.0)
Number of Subjects Censored, n (%)	82 (96.5)	164 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.647 (0.748)
95% CI		(0.149, 2.803)
Log-rank p-value		0.573

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (94.2, 100.0)	97.6 (95.2, 99.9)
6 months	93.7 (85.5, 100.0)	96.4 (93.1, 99.7)
9 months	NE (NE, NE)	96.4 (93.1, 99.7)
12 months	NE (NE, NE)	96.4 (93.1, 99.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	1 (1.2)	5 (3.0)
Number of Subjects Censored, n (%)	84 (98.8)	164 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.418 (1.096)
95% CI		(0.282, 20.702)
Log-rank p-value		0.432

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.5, 100.0)	96.9 (94.3, 99.6)
6 months	98.5 (95.5, 100.0)	96.9 (94.3, 99.6)
9 months	NE (NE, NE)	96.9 (94.3, 99.6)
12 months	NE (NE, NE)	96.9 (94.3, 99.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	1 (1.2)	1 (0.6)
Number of Subjects Censored, n (%)	84 (98.8)	168 (99.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.486 (1.416)
95% CI		(0.030, 7.799)
Log-rank p-value		0.612

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.4, 100.0)	99.4 (98.1, 100.0)
6 months	98.8 (96.4, 100.0)	99.4 (98.1, 100.0)
9 months	NE (NE, NE)	99.4 (98.1, 100.0)
12 months	NE (NE, NE)	99.4 (98.1, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	0	10 (5.9)
Number of Subjects Censored, n (%)	85 (100.0)	159 (94.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.058

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.6 (92.4, 98.8)
6 months	100.0 (100.0, 100.0)	92.8 (87.7, 97.9)
9 months	NE (NE, NE)	90.0 (82.8, 97.3)
12 months	NE (NE, NE)	90.0 (82.8, 97.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	1 (1.2)	4 (2.4)
Number of Subjects Censored, n (%)	84 (98.8)	165 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.874 (1.120)
95% CI		(0.209, 16.822)
Log-rank p-value		0.555

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.4, 100.0)	97.5 (95.0, 99.9)
6 months	98.8 (96.4, 100.0)	97.5 (95.0, 99.9)
9 months	NE (NE, NE)	97.5 (95.0, 99.9)
12 months	NE (NE, NE)	97.5 (95.0, 99.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	1 (1.2)	5 (3.0)
Number of Subjects Censored, n (%)	84 (98.8)	164 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9*, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.071 (1.107)
95% CI		(0.237, 18.112)
Log-rank p-value		0.536

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.4, 100.0)	97.5 (95.1, 99.9)
6 months	98.8 (96.4, 100.0)	95.8 (91.7, 99.9)
9 months	NE (NE, NE)	95.8 (91.7, 99.9)
12 months	NE (NE, NE)	95.8 (91.7, 99.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	1 (1.2)	3 (1.8)
Number of Subjects Censored, n (%)	84 (98.8)	166 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.517 (1.156)
95% CI		(0.158, 14.607)
Log-rank p-value		0.771

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.4, 100.0)	98.1 (96.0, 100.0)
6 months	98.8 (96.4, 100.0)	98.1 (96.0, 100.0)
9 months	NE (NE, NE)	98.1 (96.0, 100.0)
12 months	NE (NE, NE)	98.1 (96.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	0	3 (1.8)
Number of Subjects Censored, n (%)	85 (100.0)	166 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.329

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.5 (96.4, 100.0)
6 months	100.0 (100.0, 100.0)	97.4 (94.3, 100.0)
9 months	NE (NE, NE)	97.4 (94.3, 100.0)
12 months	NE (NE, NE)	97.4 (94.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	21 (24.7)	69 (40.8)
Number of Subjects Censored, n (%)	64 (75.3)	100 (59.2)
Time to first TEAE (months)		
25% percentile (95% CI)	3.55 (1.35, NE)	1.61 (0.95, 2.53)
Median (95% CI)	NE (3.71, NE)	6.90 (4.73, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.483 (0.252)
95% CI		(0.904, 2.431)
Log-rank p-value		0.113

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.7 (66.1, 85.4)	65.2 (57.8, 72.5)
6 months	64.9 (48.8, 81.1)	56.9 (48.3, 65.6)
9 months	NE (NE, NE)	46.8 (35.9, 57.8)
12 months	NE (NE, NE)	46.8 (35.9, 57.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.73	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	11 (12.9)	19 (11.2)
Number of Subjects Censored, n (%)	74 (87.1)	150 (88.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.73, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.736 (0.386)
95% CI		(0.346, 1.569)
Log-rank p-value		0.368

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.1 (75.3, 92.9)	90.8 (86.4, 95.3)
6 months	84.1 (75.3, 92.9)	86.8 (80.6, 93.0)
9 months	NE (NE, NE)	85.1 (78.2, 92.0)
12 months	NE (NE, NE)	85.1 (78.2, 92.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	2 (2.4)	15 (8.9)
Number of Subjects Censored, n (%)	83 (97.6)	154 (91.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.863 (0.758)
95% CI		(0.648, 12.651)
Log-rank p-value		0.139

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (94.3, 100.0)	92.7 (88.4, 96.9)
6 months	97.6 (94.3, 100.0)	89.5 (84.1, 94.9)
9 months	NE (NE, NE)	87.7 (81.4, 94.1)
12 months	NE (NE, NE)	87.7 (81.4, 94.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	1 (1.2)	17 (10.1)
Number of Subjects Censored, n (%)	84 (98.8)	152 (89.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.991 (1.034)
95% CI		(0.790, 45.428)
Log-rank p-value		0.044

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.4, 100.0)	92.9 (88.8, 97.0)
6 months	98.8 (96.4, 100.0)	88.7 (83.1, 94.3)
9 months	NE (NE, NE)	85.1 (77.8, 92.4)
12 months	NE (NE, NE)	85.1 (77.8, 92.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	3 (3.5)	10 (5.9)
Number of Subjects Censored, n (%)	82 (96.5)	159 (94.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.4, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.288 (0.673)
95% CI		(0.344, 4.819)
Log-rank p-value		0.693

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.4 (92.3, 100.0)	95.8 (92.7, 98.8)
6 months	96.4 (92.3, 100.0)	93.6 (89.3, 97.8)
9 months	NE (NE, NE)	90.8 (84.1, 97.6)
12 months	NE (NE, NE)	90.8 (84.1, 97.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	0	13 (7.7)
Number of Subjects Censored, n (%)	85 (100.0)	156 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.51, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.8, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.034

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.4 (90.8, 98.0)
6 months	100.0 (100.0, 100.0)	92.6 (87.6, 97.5)
9 months	NE (NE, NE)	84.0 (72.5, 95.4)
12 months	NE (NE, NE)	84.0 (72.5, 95.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	3 (3.5)	8 (4.7)
Number of Subjects Censored, n (%)	82 (96.5)	161 (95.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.021 (0.692)
95% CI		(0.263, 3.962)
Log-rank p-value		0.993

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.1 (91.6, 100.0)	96.1 (93.1, 99.2)
6 months	96.1 (91.6, 100.0)	95.1 (91.3, 98.8)
9 months	NE (NE, NE)	93.2 (88.1, 98.3)
12 months	NE (NE, NE)	93.2 (88.1, 98.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	0	4 (2.4)
Number of Subjects Censored, n (%)	85 (100.0)	165 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.210

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.2 (94.4, 99.9)
6 months	100.0 (100.0, 100.0)	97.2 (94.4, 99.9)
9 months	NE (NE, NE)	97.2 (94.4, 99.9)
12 months	NE (NE, NE)	97.2 (94.4, 99.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	2 (2.4)	6 (3.6)
Number of Subjects Censored, n (%)	83 (97.6)	163 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.55, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.008 (0.836)
95% CI		(0.196, 5.187)
Log-rank p-value		0.938

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.5, 100.0)	97.6 (95.3, 99.9)
6 months	93.5 (83.7, 100.0)	94.7 (90.1, 99.3)
9 months	NE (NE, NE)	94.7 (90.1, 99.3)
12 months	NE (NE, NE)	94.7 (90.1, 99.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	0	6 (3.6)
Number of Subjects Censored, n (%)	85 (100.0)	163 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.120

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.8 (94.0, 99.6)
6 months	100.0 (100.0, 100.0)	96.8 (94.0, 99.6)
9 months	NE (NE, NE)	94.4 (89.0, 99.8)
12 months	NE (NE, NE)	94.4 (89.0, 99.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	0	7 (4.1)
Number of Subjects Censored, n (%)	85 (100.0)	162 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.096

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.0 (92.9, 99.2)
6 months	100.0 (100.0, 100.0)	96.0 (92.9, 99.2)
9 months	NE (NE, NE)	93.6 (87.9, 99.2)
12 months	NE (NE, NE)	93.6 (87.9, 99.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	20 (23.5)	65 (38.5)
Number of Subjects Censored, n (%)	65 (76.5)	104 (61.5)
Time to first TEAE (months)		
25% percentile (95% CI)	2.40 (1.48, NE)	0.72 (0.59, 1.77)
Median (95% CI)	NE (NE, NE)	9.69 (6.41, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.689 (0.260)
95% CI		(1.015, 2.809)
Log-rank p-value		0.048

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	74.7 (65.1, 84.4)	64.2 (56.8, 71.6)
6 months	74.7 (65.1, 84.4)	60.3 (52.1, 68.5)
9 months	NE (NE, NE)	56.0 (46.4, 65.6)
12 months	NE (NE, NE)	49.8 (35.5, 64.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.46	2.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	5 (5.9)	29 (17.2)
Number of Subjects Censored, n (%)	80 (94.1)	140 (82.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.163 (0.489)
95% CI		(1.214, 8.239)
Log-rank p-value		0.014

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.8 (88.6, 99.1)	82.5 (76.7, 88.3)
6 months	93.8 (88.6, 99.1)	82.5 (76.7, 88.3)
9 months	NE (NE, NE)	82.5 (76.7, 88.3)
12 months	NE (NE, NE)	82.5 (76.7, 88.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.09

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	8 (9.4)	14 (8.3)
Number of Subjects Censored, n (%)	77 (90.6)	155 (91.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (10.28, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.2, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.636 (0.457)
95% CI		(0.260, 1.560)
Log-rank p-value		0.306

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.8 (83.0, 96.5)	93.4 (89.4, 97.4)
6 months	89.8 (83.0, 96.5)	91.3 (86.5, 96.2)
9 months	NE (NE, NE)	89.6 (83.9, 95.4)
12 months	NE (NE, NE)	80.7 (63.2, 98.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	7 (8.2)	16 (9.5)
Number of Subjects Censored, n (%)	78 (91.8)	153 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.5*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.115 (0.455)
95% CI		(0.457, 2.718)
Log-rank p-value		0.781

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (84.5, 97.4)	90.0 (85.3, 94.7)
6 months	90.9 (84.5, 97.4)	90.0 (85.3, 94.7)
9 months	NE (NE, NE)	90.0 (85.3, 94.7)
12 months	NE (NE, NE)	90.0 (85.3, 94.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	1 (1.2)	7 (4.1)
Number of Subjects Censored, n (%)	84 (98.8)	162 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.386 (1.070)
95% CI		(0.416, 27.545)
Log-rank p-value		0.240

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.4, 100.0)	95.6 (92.4, 98.8)
6 months	98.8 (96.4, 100.0)	95.6 (92.4, 98.8)
9 months	NE (NE, NE)	95.6 (92.4, 98.8)
12 months	NE (NE, NE)	95.6 (92.4, 98.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	1 (1.2)	2 (1.2)
Number of Subjects Censored, n (%)	84 (98.8)	167 (98.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.5, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.987 (1.226)
95% CI		(0.089, 10.911)
Log-rank p-value		0.993

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	98.8 (97.2, 100.0)
6 months	98.6 (96.0, 100.0)	98.8 (97.2, 100.0)
9 months	NE (NE, NE)	98.8 (97.2, 100.0)
12 months	NE (NE, NE)	98.8 (97.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Vascular disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	11 (12.9)	66 (39.1)
Number of Subjects Censored, n (%)	74 (87.1)	103 (60.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.61, NE)	0.95 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	NE (6.93, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.220 (0.327)
95% CI		(1.695, 6.116)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Vascular disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.7 (78.8, 94.5)	63.2 (55.8, 70.6)
6 months	80.5 (66.7, 94.2)	59.0 (50.7, 67.3)
9 months	NE (NE, NE)	52.2 (40.6, 63.7)
12 months	NE (NE, NE)	52.2 (40.6, 63.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	7 (8.2)	64 (37.9)
Number of Subjects Censored, n (%)	78 (91.8)	105 (62.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.99 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	NE (6.93, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.040 (0.399)
95% CI		(2.304, 11.022)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.5 (83.7, 97.3)	63.7 (56.3, 71.1)
6 months	90.5 (83.7, 97.3)	60.8 (52.7, 68.9)
9 months	NE (NE, NE)	53.8 (42.1, 65.4)
12 months	NE (NE, NE)	53.8 (42.1, 65.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	26 (30.6)	60 (35.5)
Number of Subjects Censored, n (%)	59 (69.4)	109 (64.5)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.69, 3.71)	1.71 (0.79, 2.56)
Median (95% CI)	NE (3.71, NE)	NE (7.66, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.044 (0.238)
95% CI		(0.655, 1.664)
Log-rank p-value		0.734

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	68.9 (58.2, 79.6)	66.1 (58.7, 73.4)
6 months	58.3 (42.0, 74.6)	60.4 (51.7, 69.1)
9 months	NE (NE, NE)	56.7 (45.8, 67.5)
12 months	NE (NE, NE)	56.7 (45.8, 67.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.53	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	9 (10.6)	17 (10.1)
Number of Subjects Censored, n (%)	76 (89.4)	152 (89.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.843 (0.415)
95% CI		(0.374, 1.901)
Log-rank p-value		0.805

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.0 (82.2, 95.8)	89.8 (85.1, 94.6)
6 months	89.0 (82.2, 95.8)	88.8 (83.7, 93.9)
9 months	NE (NE, NE)	88.8 (83.7, 93.9)
12 months	NE (NE, NE)	88.8 (83.7, 93.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	5 (5.9)	26 (15.4)
Number of Subjects Censored, n (%)	80 (94.1)	143 (84.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.98, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.1, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.312 (0.493)
95% CI		(0.881, 6.071)
Log-rank p-value		0.086

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.9 (88.6, 99.1)	87.1 (81.9, 92.3)
6 months	93.9 (88.6, 99.1)	81.1 (73.4, 88.8)
9 months	NE (NE, NE)	77.3 (66.9, 87.7)
12 months	NE (NE, NE)	77.3 (66.9, 87.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	3 (3.5)	4 (2.4)
Number of Subjects Censored, n (%)	82 (96.5)	165 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.449 (0.783)
95% CI		(0.097, 2.084)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.5, 100.0)	98.1 (96.0, 100.0)
6 months	88.9 (75.8, 100.0)	96.6 (92.9, 100.0)
9 months	NE (NE, NE)	96.6 (92.9, 100.0)
12 months	NE (NE, NE)	96.6 (92.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	2 (2.4)	6 (3.6)
Number of Subjects Censored, n (%)	83 (97.6)	163 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.505 (0.818)
95% CI		(0.303, 7.487)
Log-rank p-value		0.661

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (94.3, 100.0)	96.2 (93.2, 99.2)
6 months	97.6 (94.3, 100.0)	96.2 (93.2, 99.2)
9 months	NE (NE, NE)	96.2 (93.2, 99.2)
12 months	NE (NE, NE)	96.2 (93.2, 99.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	1 (1.2)	2 (1.2)
Number of Subjects Censored, n (%)	84 (98.8)	167 (98.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.8, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.904 (1.225)
95% CI		(0.082, 9.970)
Log-rank p-value		0.934

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.4, 100.0)	98.8 (97.1, 100.0)
6 months	98.8 (96.4, 100.0)	98.8 (97.1, 100.0)
9 months	NE (NE, NE)	98.8 (97.1, 100.0)
12 months	NE (NE, NE)	98.8 (97.1, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	0	3 (1.8)
Number of Subjects Censored, n (%)	85 (100.0)	166 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.8, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.303

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.0 (95.7, 100.0)
6 months	100.0 (100.0, 100.0)	98.0 (95.7, 100.0)
9 months	NE (NE, NE)	98.0 (95.7, 100.0)
12 months	NE (NE, NE)	98.0 (95.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	10 (11.8)	55 (32.5)
Number of Subjects Censored, n (%)	75 (88.2)	114 (67.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.61 (0.95, 3.71)
Median (95% CI)	NE (NE, NE)	13.14 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	13.14 (NE, NE)
Min, Max	0.1, 6.8*	0.0, 13.1
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.985 (0.345)
95% CI		(1.518, 5.872)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.8 (80.7, 94.9)	68.9 (61.8, 76.0)
6 months	87.8 (80.7, 94.9)	64.5 (56.2, 72.8)
9 months	NE (NE, NE)	64.5 (56.2, 72.8)
12 months	NE (NE, NE)	64.5 (56.2, 72.8)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.79	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	3 (3.5)	28 (16.6)
Number of Subjects Censored, n (%)	82 (96.5)	141 (83.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.86, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.116 (0.609)
95% CI		(1.552, 16.862)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.3 (92.2, 100.0)	83.9 (78.3, 89.6)
6 months	96.3 (92.2, 100.0)	81.2 (74.5, 87.9)
9 months	NE (NE, NE)	81.2 (74.5, 87.9)
12 months	NE (NE, NE)	81.2 (74.5, 87.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	4 (4.7)	7 (4.1)
Number of Subjects Censored, n (%)	81 (95.3)	162 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.860 (0.627)
95% CI		(0.251, 2.942)
Log-rank p-value		0.830

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.2 (90.6, 99.8)	95.8 (92.7, 98.8)
6 months	95.2 (90.6, 99.8)	95.8 (92.7, 98.8)
9 months	NE (NE, NE)	95.8 (92.7, 98.8)
12 months	NE (NE, NE)	95.8 (92.7, 98.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	0	5 (3.0)
Number of Subjects Censored, n (%)	85 (100.0)	164 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.150

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.5 (95.0, 99.9)
6 months	100.0 (100.0, 100.0)	96.5 (93.3, 99.6)
9 months	NE (NE, NE)	96.5 (93.3, 99.6)
12 months	NE (NE, NE)	96.5 (93.3, 99.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Nervous system disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	10 (11.8)	40 (23.7)
Number of Subjects Censored, n (%)	75 (88.2)	129 (76.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.32 (1.61, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.928 (0.356)
95% CI		(0.959, 3.875)
Log-rank p-value		0.075

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Nervous system disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.1 (79.6, 94.7)	77.9 (71.4, 84.3)
6 months	87.1 (79.6, 94.7)	72.1 (63.9, 80.3)
9 months	NE (NE, NE)	72.1 (63.9, 80.3)
12 months	NE (NE, NE)	72.1 (63.9, 80.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	4 (4.7)	12 (7.1)
Number of Subjects Censored, n (%)	81 (95.3)	157 (92.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.548 (0.578)
95% CI		(0.499, 4.804)
Log-rank p-value		0.453

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (90.4, 99.8)	92.8 (88.9, 96.7)
6 months	95.1 (90.4, 99.8)	92.8 (88.9, 96.7)
9 months	NE (NE, NE)	92.8 (88.9, 96.7)
12 months	NE (NE, NE)	92.8 (88.9, 96.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	1 (1.2)	4 (2.4)
Number of Subjects Censored, n (%)	84 (98.8)	165 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.4, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.954 (1.119)
95% CI		(0.218, 17.507)
Log-rank p-value		0.541

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.4, 100.0)	97.5 (95.2, 99.9)
6 months	98.8 (96.4, 100.0)	97.5 (95.2, 99.9)
9 months	NE (NE, NE)	97.5 (95.2, 99.9)
12 months	NE (NE, NE)	97.5 (95.2, 99.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	1 (1.2)	2 (1.2)
Number of Subjects Censored, n (%)	84 (98.8)	167 (98.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.019 (1.226)
95% CI		(0.092, 11.264)
Log-rank p-value		0.974

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.2, 100.0)	98.8 (97.2, 100.0)
6 months	98.7 (96.2, 100.0)	98.8 (97.2, 100.0)
9 months	NE (NE, NE)	98.8 (97.2, 100.0)
12 months	NE (NE, NE)	98.8 (97.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	13 (15.3)	42 (24.9)
Number of Subjects Censored, n (%)	72 (84.7)	127 (75.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.87, NE)	5.06 (2.76, NE)
Median (95% CI)	NE (NE, NE)	13.60 (11.96, NE)
75% percentile (95% CI)	NE (NE, NE)	13.60 (11.96, NE)
Min, Max	0.0, 6.8*	0.1, 13.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.251 (0.324)
95% CI		(0.664, 2.359)
Log-rank p-value		0.605

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.5 (75.3, 91.7)	81.5 (75.5, 87.5)
6 months	83.5 (75.3, 91.7)	70.4 (61.6, 79.1)
9 months	NE (NE, NE)	67.8 (58.0, 77.6)
12 months	NE (NE, NE)	50.8 (21.1, 80.5)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.73	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	6 (7.1)	26 (15.4)
Number of Subjects Censored, n (%)	79 (92.9)	143 (84.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	8.38 (5.78, NE)
Median (95% CI)	NE (NE, NE)	13.60 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	13.60 (NE, NE)
Min, Max	0.2*, 6.8*	0.5, 13.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.490 (0.464)
95% CI		(0.600, 3.701)
Log-rank p-value		0.398

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (86.4, 98.2)	89.9 (85.3, 94.6)
6 months	92.3 (86.4, 98.2)	81.5 (73.9, 89.0)
9 months	NE (NE, NE)	74.5 (62.8, 86.3)
12 months	NE (NE, NE)	74.5 (62.8, 86.3)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	3 (3.5)	6 (3.6)
Number of Subjects Censored, n (%)	82 (96.5)	163 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.856 (0.712)
95% CI		(0.212, 3.457)
Log-rank p-value		0.740

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.3 (92.1, 100.0)	97.0 (94.3, 99.6)
6 months	96.3 (92.1, 100.0)	95.8 (92.5, 99.2)
9 months	NE (NE, NE)	95.8 (92.5, 99.2)
12 months	NE (NE, NE)	95.8 (92.5, 99.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Infections and infestations**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	13 (15.3)	39 (23.1)
Number of Subjects Censored, n (%)	72 (84.7)	130 (76.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.15, NE)	5.78 (3.52, 7.69)
Median (95% CI)	NE (NE, NE)	NE (7.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.025 (0.331)
95% CI		(0.535, 1.963)
Log-rank p-value		0.826

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Infections and infestations**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.8 (78.0, 93.6)	83.2 (77.2, 89.2)
6 months	76.6 (62.4, 90.8)	72.6 (63.8, 81.5)
9 months	NE (NE, NE)	58.3 (44.5, 72.1)
12 months	NE (NE, NE)	58.3 (44.5, 72.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	3 (3.5)	8 (4.7)
Number of Subjects Censored, n (%)	82 (96.5)	161 (95.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.4, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.832 (0.706)
95% CI		(0.208, 3.323)
Log-rank p-value		0.953

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.2 (93.3, 99.2)
6 months	82.9 (64.1, 100.0)	96.2 (93.3, 99.2)
9 months	NE (NE, NE)	91.8 (85.0, 98.5)
12 months	NE (NE, NE)	91.8 (85.0, 98.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	5 (5.9)	3 (1.8)
Number of Subjects Censored, n (%)	80 (94.1)	166 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.209 (0.760)
95% CI		(0.047, 0.927)
Log-rank p-value		0.018

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.5 (88.0, 99.0)	99.4 (98.3, 100.0)
6 months	93.5 (88.0, 99.0)	96.6 (92.5, 100.0)
9 months	NE (NE, NE)	96.6 (92.5, 100.0)
12 months	NE (NE, NE)	96.6 (92.5, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	0	3 (1.8)
Number of Subjects Censored, n (%)	85 (100.0)	166 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.247

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.0 (95.6, 100.0)
6 months	100.0 (100.0, 100.0)	98.0 (95.6, 100.0)
9 months	NE (NE, NE)	98.0 (95.6, 100.0)
12 months	NE (NE, NE)	98.0 (95.6, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	15 (17.6)	26 (15.4)
Number of Subjects Censored, n (%)	70 (82.4)	143 (84.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.84, NE)	NE (5.85, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.679 (0.332)
95% CI		(0.354, 1.302)
Log-rank p-value		0.282

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.1 (70.8, 89.3)	88.5 (83.6, 93.4)
6 months	80.1 (70.8, 89.3)	82.5 (75.5, 89.5)
9 months	NE (NE, NE)	78.7 (70.3, 87.1)
12 months	NE (NE, NE)	78.7 (70.3, 87.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	13 (15.3)	13 (7.7)
Number of Subjects Censored, n (%)	72 (84.7)	156 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.79, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.314 (0.411)
95% CI		(0.140, 0.702)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.2 (73.2, 91.2)	96.3 (93.4, 99.2)
6 months	82.2 (73.2, 91.2)	89.9 (83.6, 96.2)
9 months	NE (NE, NE)	86.2 (78.4, 94.0)
12 months	NE (NE, NE)	86.2 (78.4, 94.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	2 (2.4)	11 (6.5)
Number of Subjects Censored, n (%)	83 (97.6)	158 (93.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.675 (0.769)
95% CI		(0.592, 12.075)
Log-rank p-value		0.178

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (94.1, 100.0)	93.4 (89.7, 97.2)
6 months	97.5 (94.1, 100.0)	93.4 (89.7, 97.2)
9 months	NE (NE, NE)	93.4 (89.7, 97.2)
12 months	NE (NE, NE)	93.4 (89.7, 97.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Endocrine disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	0	38 (22.5)
Number of Subjects Censored, n (%)	85 (100.0)	131 (77.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	6.01 (2.10, NE)
Median (95% CI)	NE (NE, NE)	NE (9.33, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Endocrine disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	78.4 (72.0, 84.9)
6 months	100.0 (100.0, 100.0)	75.9 (68.7, 83.0)
9 months	NE (NE, NE)	73.7 (65.6, 81.8)
12 months	NE (NE, NE)	65.5 (48.7, 82.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	0	34 (20.1)
Number of Subjects Censored, n (%)	85 (100.0)	135 (79.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	9.33 (2.76, NE)
Median (95% CI)	NE (NE, NE)	NE (9.33, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	81.0 (74.8, 87.1)
6 months	100.0 (100.0, 100.0)	78.4 (71.5, 85.3)
9 months	NE (NE, NE)	76.3 (68.4, 84.2)
12 months	NE (NE, NE)	68.7 (52.8, 84.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Psychiatric disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	7 (8.2)	24 (14.2)
Number of Subjects Censored, n (%)	78 (91.8)	145 (85.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.90, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.413 (0.432)
95% CI		(0.606, 3.297)
Log-rank p-value		0.406

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Psychiatric disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.2 (86.1, 98.2)	87.4 (81.9, 92.8)
6 months	88.5 (79.3, 97.6)	81.7 (74.7, 88.7)
9 months	NE (NE, NE)	81.7 (74.7, 88.7)
12 months	NE (NE, NE)	81.7 (74.7, 88.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	5 (5.9)	13 (7.7)
Number of Subjects Censored, n (%)	80 (94.1)	156 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.041 (0.529)
95% CI		(0.369, 2.939)
Log-rank p-value		0.848

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.3 (87.7, 99.0)	93.1 (88.9, 97.3)
6 months	93.3 (87.7, 99.0)	90.0 (84.6, 95.3)
9 months	NE (NE, NE)	90.0 (84.6, 95.3)
12 months	NE (NE, NE)	90.0 (84.6, 95.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	2 (2.4)	6 (3.6)
Number of Subjects Censored, n (%)	83 (97.6)	163 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.092 (0.824)
95% CI		(0.217, 5.494)
Log-rank p-value		0.965

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.1, 100.0)	96.4 (93.2, 99.6)
6 months	94.9 (87.2, 100.0)	94.9 (90.6, 99.2)
9 months	NE (NE, NE)	94.9 (90.6, 99.2)
12 months	NE (NE, NE)	94.9 (90.6, 99.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	1 (1.2)	0
Number of Subjects Censored, n (%)	84 (98.8)	169 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.143

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.4, 100.0)	100.0 (100.0, 100.0)
6 months	98.8 (96.4, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	12 (14.1)	21 (12.4)
Number of Subjects Censored, n (%)	73 (85.9)	148 (87.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.15, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.772 (0.364)
95% CI		(0.378, 1.575)
Log-rank p-value		0.456

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.6 (79.2, 94.0)	87.4 (82.2, 92.6)
6 months	83.1 (73.4, 92.9)	85.8 (79.8, 91.7)
9 months	NE (NE, NE)	85.8 (79.8, 91.7)
12 months	NE (NE, NE)	85.8 (79.8, 91.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	1 (1.2)	7 (4.1)
Number of Subjects Censored, n (%)	84 (98.8)	162 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.862 (1.077)
95% CI		(0.347, 23.602)
Log-rank p-value		0.332

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.1, 100.0)	96.0 (92.8, 99.1)
6 months	98.7 (96.1, 100.0)	94.3 (89.8, 98.8)
9 months	NE (NE, NE)	94.3 (89.8, 98.8)
12 months	NE (NE, NE)	94.3 (89.8, 98.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Number of Subjects with Events, n (%)	1 (1.2)	6 (3.6)
Number of Subjects Censored, n (%)	84 (98.8)	163 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.961 (1.081)
95% CI		(0.356, 24.617)
Log-rank p-value		0.291

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=85	Fruquintinib + BSC N=169
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.4, 100.0)	96.4 (93.5, 99.2)
6 months	98.8 (96.4, 100.0)	96.4 (93.5, 99.2)
9 months	NE (NE, NE)	96.4 (93.5, 99.2)
12 months	NE (NE, NE)	96.4 (93.5, 99.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	74 (51.0)	194 (67.6)
Number of Subjects Censored, n (%)	71 (49.0)	93 (32.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.49, 0.72)	0.59 (0.36, 0.69)
Median (95% CI)	2.76 (1.41, NE)	1.35 (0.95, 1.64)
75% percentile (95% CI)	NE (NE, NE)	NE (4.47, NE)
Min, Max	0.0, 13.0*	0.0, 12.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.374 (0.138)
95% CI		(1.048, 1.801)
Log-rank p-value		0.030

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	48.0 (39.5, 56.4)	37.4 (31.7, 43.1)
6 months	45.4 (36.1, 54.8)	26.5 (20.4, 32.5)
9 months	45.4 (36.1, 54.8)	26.5 (20.4, 32.5)
12 months	45.4 (36.1, 54.8)	26.5 (20.4, 32.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.68	1.28

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	28 (19.3)	92 (32.1)
Number of Subjects Censored, n (%)	117 (80.7)	195 (67.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.87, NE)	1.61 (0.92, 2.89)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.588 (0.217)
95% CI		(1.038, 2.431)
Log-rank p-value		0.029

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.4 (73.6, 87.1)	69.9 (64.5, 75.4)
6 months	77.1 (68.2, 86.1)	65.6 (59.6, 71.6)
9 months	77.1 (68.2, 86.1)	62.3 (53.9, 70.8)
12 months	77.1 (68.2, 86.1)	62.3 (53.9, 70.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.53	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	22 (15.2)	55 (19.2)
Number of Subjects Censored, n (%)	123 (84.8)	232 (80.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.71, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.144 (0.256)
95% CI		(0.692, 1.891)
Log-rank p-value		0.621

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.8 (77.6, 90.1)	81.3 (76.7, 85.9)
6 months	83.8 (77.6, 90.1)	79.0 (73.8, 84.2)
9 months	83.8 (77.6, 90.1)	79.0 (73.8, 84.2)
12 months	83.8 (77.6, 90.1)	79.0 (73.8, 84.2)
18 months	NE (NE, NE)	79.0 (73.8, 84.2)
Median Follow-up Time (months)	2.46	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	13 (9.0)	22 (7.7)
Number of Subjects Censored, n (%)	132 (91.0)	265 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.689 (0.361)
95% CI		(0.340, 1.397)
Log-rank p-value		0.319

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (84.7, 95.3)	93.5 (90.6, 96.4)
6 months	90.0 (84.7, 95.3)	91.9 (88.2, 95.5)
9 months	90.0 (84.7, 95.3)	90.7 (86.3, 95.0)
12 months	90.0 (84.7, 95.3)	83.1 (68.4, 97.8)
18 months	NE (NE, NE)	83.1 (68.4, 97.8)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	5 (3.4)	42 (14.6)
Number of Subjects Censored, n (%)	140 (96.6)	245 (85.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
Median (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.24, NE)
Min, Max	0.4*, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.119 (0.475)
95% CI		(1.624, 10.449)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.2 (92.9, 99.5)	86.5 (82.5, 90.5)
6 months	96.2 (92.9, 99.5)	85.0 (80.6, 89.5)
9 months	96.2 (92.9, 99.5)	83.5 (78.2, 88.8)
12 months	96.2 (92.9, 99.5)	83.5 (78.2, 88.8)
18 months	NE (NE, NE)	41.7 (0.0, 99.6)
Median Follow-up Time (months)	2.79	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	17 (11.7)	18 (6.3)
Number of Subjects Censored, n (%)	128 (88.3)	269 (93.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.388 (0.348)
95% CI		(0.196, 0.768)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.1 (81.4, 92.9)	96.0 (93.7, 98.3)
6 months	87.1 (81.4, 92.9)	91.8 (87.7, 95.9)
9 months	87.1 (81.4, 92.9)	91.8 (87.7, 95.9)
12 months	87.1 (81.4, 92.9)	91.8 (87.7, 95.9)
18 months	NE (NE, NE)	80.3 (59.0, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	12 (8.3)	16 (5.6)
Number of Subjects Censored, n (%)	133 (91.7)	271 (94.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.592 (0.387)
95% CI		(0.277, 1.264)
Log-rank p-value		0.172

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.0 (86.1, 96.0)	94.6 (91.9, 97.2)
6 months	91.0 (86.1, 96.0)	94.6 (91.9, 97.2)
9 months	91.0 (86.1, 96.0)	94.6 (91.9, 97.2)
12 months	91.0 (86.1, 96.0)	90.4 (82.2, 98.7)
18 months	NE (NE, NE)	90.4 (82.2, 98.7)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	3 (2.1)	7 (2.4)
Number of Subjects Censored, n (%)	142 (97.9)	280 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.879 (0.708)
95% CI		(0.219, 3.521)
Log-rank p-value		0.865

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.9 (95.6, 100.0)	98.1 (96.5, 99.8)
6 months	97.9 (95.6, 100.0)	97.6 (95.7, 99.5)
9 months	97.9 (95.6, 100.0)	97.6 (95.7, 99.5)
12 months	97.9 (95.6, 100.0)	93.5 (85.5, 100.0)
18 months	NE (NE, NE)	93.5 (85.5, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	3 (2.1)	5 (1.7)
Number of Subjects Censored, n (%)	142 (97.9)	282 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.574 (0.749)
95% CI		(0.132, 2.492)
Log-rank p-value		0.420

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (95.2, 100.0)	98.9 (97.6, 100.0)
6 months	97.7 (95.2, 100.0)	97.3 (94.9, 99.8)
9 months	97.7 (95.2, 100.0)	97.3 (94.9, 99.8)
12 months	97.7 (95.2, 100.0)	97.3 (94.9, 99.8)
18 months	NE (NE, NE)	97.3 (94.9, 99.8)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	2 (1.4)	7 (2.4)
Number of Subjects Censored, n (%)	143 (98.6)	280 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.374 (0.825)
95% CI		(0.273, 6.915)
Log-rank p-value		0.661

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.7, 100.0)	98.2 (96.7, 99.8)
6 months	98.6 (96.7, 100.0)	97.0 (94.2, 99.8)
9 months	98.6 (96.7, 100.0)	94.2 (88.0, 100.0)
12 months	98.6 (96.7, 100.0)	94.2 (88.0, 100.0)
18 months	NE (NE, NE)	94.2 (88.0, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	75 (51.7)	196 (68.3)
Number of Subjects Censored, n (%)	70 (48.3)	91 (31.7)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.46, 0.72)	0.56 (0.46, 0.69)
Median (95% CI)	2.00 (1.38, 5.59)	1.45 (0.92, 1.94)
75% percentile (95% CI)	5.59 (5.36, NE)	5.55 (4.86, 10.12)
Min, Max	0.0, 6.4*	0.0, 11.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.266 (0.139)
95% CI		(0.964, 1.662)
Log-rank p-value		0.083

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	46.9 (38.2, 55.6)	39.2 (33.4, 45.0)
6 months	20.9 (0.0, 42.2)	24.2 (17.7, 30.8)
9 months	NE (NE, NE)	17.8 (10.5, 25.1)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.54	1.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	16 (11.0)	68 (23.7)
Number of Subjects Censored, n (%)	129 (89.0)	219 (76.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.55 (2.56, NE)
Median (95% CI)	NE (NE, NE)	NE (10.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.949 (0.282)
95% CI		(1.121, 3.389)
Log-rank p-value		0.017

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.5 (83.2, 93.8)	79.5 (74.7, 84.3)
6 months	88.5 (83.2, 93.8)	73.5 (67.3, 79.6)
9 months	88.5 (83.2, 93.8)	70.2 (62.8, 77.6)
12 months	88.5 (83.2, 93.8)	63.2 (48.5, 77.8)
18 months	NE (NE, NE)	63.2 (48.5, 77.8)
Median Follow-up Time (months)	2.56	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	24 (16.6)	47 (16.4)
Number of Subjects Censored, n (%)	121 (83.4)	240 (83.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (5.55, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.787 (0.260)
95% CI		(0.472, 1.311)
Log-rank p-value		0.295

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.2 (76.8, 89.5)	86.2 (82.0, 90.4)
6 months	77.6 (65.5, 89.7)	79.4 (73.4, 85.4)
9 months	77.6 (65.5, 89.7)	76.1 (68.6, 83.5)
12 months	77.6 (65.5, 89.7)	76.1 (68.6, 83.5)
18 months	NE (NE, NE)	76.1 (68.6, 83.5)
Median Follow-up Time (months)	2.63	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	20 (13.8)	54 (18.8)
Number of Subjects Censored, n (%)	125 (86.2)	233 (81.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	10.12 (4.83, NE)
Median (95% CI)	NE (NE, NE)	NE (12.25, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.072 (0.269)
95% CI		(0.633, 1.816)
Log-rank p-value		0.657

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.1 (79.0, 91.2)	83.7 (79.2, 88.2)
6 months	85.1 (79.0, 91.2)	78.2 (72.4, 84.1)
9 months	85.1 (79.0, 91.2)	75.9 (69.3, 82.4)
12 months	85.1 (79.0, 91.2)	71.9 (62.1, 81.7)
18 months	NE (NE, NE)	59.9 (37.0, 82.8)
Median Follow-up Time (months)	2.63	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	8 (5.5)	47 (16.4)
Number of Subjects Censored, n (%)	137 (94.5)	240 (83.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	9.33 (6.70, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.542 (0.405)
95% CI		(1.149, 5.621)
Log-rank p-value		0.024

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (90.6, 98.2)	86.3 (82.1, 90.5)
6 months	94.4 (90.6, 98.2)	81.3 (75.8, 86.7)
9 months	94.4 (90.6, 98.2)	76.2 (68.6, 83.8)
12 months	94.4 (90.6, 98.2)	73.1 (63.8, 82.5)
18 months	NE (NE, NE)	73.1 (63.8, 82.5)
Median Follow-up Time (months)	2.79	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	18 (12.4)	39 (13.6)
Number of Subjects Censored, n (%)	127 (87.6)	248 (86.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.36, NE)	18.04 (7.10, NE)
Median (95% CI)	NE (NE, NE)	NE (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.897 (0.302)
95% CI		(0.496, 1.621)
Log-rank p-value		0.804

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (81.8, 93.1)	89.7 (86.1, 93.4)
6 months	78.7 (61.7, 95.7)	83.4 (77.9, 88.9)
9 months	78.7 (61.7, 95.7)	80.4 (73.7, 87.2)
12 months	78.7 (61.7, 95.7)	80.4 (73.7, 87.2)
18 months	NE (NE, NE)	80.4 (73.7, 87.2)
Median Follow-up Time (months)	2.79	3.42

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	1 (0.7)	39 (13.6)
Number of Subjects Censored, n (%)	144 (99.3)	248 (86.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		25.172 (1.052)
95% CI		(3.199, 198.041)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	87.5 (83.6, 91.4)
6 months	99.3 (97.8, 100.0)	85.3 (80.7, 89.8)
9 months	99.3 (97.8, 100.0)	83.7 (78.3, 89.1)
12 months	99.3 (97.8, 100.0)	83.7 (78.3, 89.1)
18 months	NE (NE, NE)	83.7 (78.3, 89.1)
Median Follow-up Time (months)	2.83	3.48

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	6 (4.1)	23 (8.0)
Number of Subjects Censored, n (%)	139 (95.9)	264 (92.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.555 (0.465)
95% CI		(0.625, 3.871)
Log-rank p-value		0.358

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.4 (93.4, 99.5)	93.4 (90.5, 96.4)
6 months	84.4 (62.1, 100.0)	89.6 (85.2, 94.0)
9 months	NE (NE, NE)	89.6 (85.2, 94.0)
12 months	NE (NE, NE)	89.6 (85.2, 94.0)
18 months	NE (NE, NE)	89.6 (85.2, 94.0)
Median Follow-up Time (months)	2.83	3.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	2 (1.4)	10 (3.5)
Number of Subjects Censored, n (%)	143 (98.6)	277 (96.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.022 (0.813)
95% CI		(0.411, 9.956)
Log-rank p-value		0.336

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.7, 100.0)	97.5 (95.7, 99.3)
6 months	98.6 (96.7, 100.0)	95.7 (92.6, 98.8)
9 months	98.6 (96.7, 100.0)	93.7 (88.7, 98.7)
12 months	98.6 (96.7, 100.0)	93.7 (88.7, 98.7)
18 months	NE (NE, NE)	93.7 (88.7, 98.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	3 (2.1)	7 (2.4)
Number of Subjects Censored, n (%)	142 (97.9)	280 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.205 (0.695)
95% CI		(0.309, 4.706)
Log-rank p-value		0.782

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (94.6, 100.0)	97.5 (95.7, 99.3)
6 months	97.5 (94.6, 100.0)	97.5 (95.7, 99.3)
9 months	97.5 (94.6, 100.0)	97.5 (95.7, 99.3)
12 months	97.5 (94.6, 100.0)	97.5 (95.7, 99.3)
18 months	NE (NE, NE)	97.5 (95.7, 99.3)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	6 (4.1)	2 (0.7)
Number of Subjects Censored, n (%)	139 (95.9)	285 (99.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.111 (0.874)
95% CI		(0.020, 0.618)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.8 (92.5, 99.1)	99.6 (98.9, 100.0)
6 months	95.8 (92.5, 99.1)	98.5 (96.1, 100.0)
9 months	95.8 (92.5, 99.1)	98.5 (96.1, 100.0)
12 months	95.8 (92.5, 99.1)	98.5 (96.1, 100.0)
18 months	NE (NE, NE)	98.5 (96.1, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	0	5 (1.7)
Number of Subjects Censored, n (%)	145 (100.0)	282 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.168

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.5 (97.1, 100.0)
6 months	100.0 (100.0, 100.0)	98.5 (97.1, 100.0)
9 months	100.0 (100.0, 100.0)	96.3 (91.7, 100.0)
12 months	100.0 (100.0, 100.0)	96.3 (91.7, 100.0)
18 months	NE (NE, NE)	96.3 (91.7, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	36 (24.8)	126 (43.9)
Number of Subjects Censored, n (%)	109 (75.2)	161 (56.1)
Time to first TEAE (months)		
25% percentile (95% CI)	4.27 (0.95, NE)	1.35 (0.82, 1.64)
Median (95% CI)	10.18 (NE, NE)	6.24 (3.68, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.0, 10.2	0.0, 12.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.592 (0.193)
95% CI		(1.091, 2.323)
Log-rank p-value		0.012

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.1 (67.7, 82.5)	58.7 (52.7, 64.6)
6 months	68.9 (55.3, 82.4)	51.8 (45.0, 58.7)
9 months	68.9 (55.3, 82.4)	46.9 (39.2, 54.6)
12 months	0.0 (NE, NE)	43.0 (32.8, 53.2)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.46	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	20 (13.8)	76 (26.5)
Number of Subjects Censored, n (%)	125 (86.2)	211 (73.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.27, NE)	2.99 (1.84, 9.43)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.792 (0.256)
95% CI		(1.084, 2.962)
Log-rank p-value		0.022

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.7 (79.7, 91.7)	74.5 (69.2, 79.8)
6 months	80.0 (67.8, 92.2)	71.6 (65.8, 77.4)
9 months	80.0 (67.8, 92.2)	69.2 (62.6, 75.7)
12 months	80.0 (67.8, 92.2)	65.9 (57.0, 74.7)
18 months	NE (NE, NE)	65.9 (57.0, 74.7)
Median Follow-up Time (months)	2.60	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	3 (2.1)	21 (7.3)
Number of Subjects Censored, n (%)	142 (97.9)	266 (92.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.322 (0.640)
95% CI		(0.947, 11.646)
Log-rank p-value		0.063

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.9 (95.6, 100.0)	92.8 (89.6, 95.9)
6 months	97.9 (95.6, 100.0)	91.4 (87.7, 95.0)
9 months	97.9 (95.6, 100.0)	91.4 (87.7, 95.0)
12 months	97.9 (95.6, 100.0)	91.4 (87.7, 95.0)
18 months	NE (NE, NE)	91.4 (87.7, 95.0)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	2 (1.4)	15 (5.2)
Number of Subjects Censored, n (%)	143 (98.6)	272 (94.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.495 (0.765)
95% CI		(0.558, 11.164)
Log-rank p-value		0.225

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.7, 100.0)	95.9 (93.5, 98.3)
6 months	98.6 (96.7, 100.0)	93.3 (89.5, 97.0)
9 months	98.6 (96.7, 100.0)	91.4 (86.3, 96.6)
12 months	98.6 (96.7, 100.0)	91.4 (86.3, 96.6)
18 months	NE (NE, NE)	91.4 (86.3, 96.6)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	3 (2.1)	9 (3.1)
Number of Subjects Censored, n (%)	142 (97.9)	278 (96.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.183 (0.680)
95% CI		(0.312, 4.484)
Log-rank p-value		0.759

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.9 (95.6, 100.0)	97.3 (95.4, 99.3)
6 months	97.9 (95.6, 100.0)	96.7 (94.4, 99.0)
9 months	97.9 (95.6, 100.0)	93.9 (88.1, 99.7)
12 months	97.9 (95.6, 100.0)	93.9 (88.1, 99.7)
18 months	NE (NE, NE)	93.9 (88.1, 99.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	2 (1.4)	14 (4.9)
Number of Subjects Censored, n (%)	143 (98.6)	273 (95.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.369 (0.771)
95% CI		(0.743, 15.274)
Log-rank p-value		0.110

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.7, 100.0)	95.5 (93.0, 98.0)
6 months	98.6 (96.7, 100.0)	94.5 (91.4, 97.6)
9 months	98.6 (96.7, 100.0)	92.7 (87.9, 97.4)
12 months	98.6 (96.7, 100.0)	92.7 (87.9, 97.4)
18 months	NE (NE, NE)	92.7 (87.9, 97.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	0	8 (2.8)
Number of Subjects Censored, n (%)	145 (100.0)	279 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.084

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.5 (95.6, 99.3)
6 months	100.0 (100.0, 100.0)	96.7 (94.2, 99.1)
9 months	100.0 (100.0, 100.0)	96.7 (94.2, 99.1)
12 months	100.0 (100.0, 100.0)	96.7 (94.2, 99.1)
18 months	NE (NE, NE)	96.7 (94.2, 99.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	2 (1.4)	9 (3.1)
Number of Subjects Censored, n (%)	143 (98.6)	278 (96.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.765 (0.790)
95% CI		(0.376, 8.296)
Log-rank p-value		0.465

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.9 (94.9, 100.0)	97.0 (94.9, 99.1)
6 months	97.9 (94.9, 100.0)	97.0 (94.9, 99.1)
9 months	97.9 (94.9, 100.0)	95.7 (92.4, 98.9)
12 months	97.9 (94.9, 100.0)	95.7 (92.4, 98.9)
18 months	NE (NE, NE)	95.7 (92.4, 98.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	1 (0.7)	8 (2.8)
Number of Subjects Censored, n (%)	144 (99.3)	279 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.720 (1.079)
95% CI		(0.328, 22.556)
Log-rank p-value		0.295

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	98.1 (96.5, 99.8)
6 months	99.3 (97.9, 100.0)	97.6 (95.6, 99.5)
9 months	99.3 (97.9, 100.0)	93.6 (87.6, 99.6)
12 months	99.3 (97.9, 100.0)	93.6 (87.6, 99.6)
18 months	NE (NE, NE)	93.6 (87.6, 99.6)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	2 (1.4)	8 (2.8)
Number of Subjects Censored, n (%)	143 (98.6)	279 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Median (95% CI)	10.18 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 10.2	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.367 (0.817)
95% CI		(0.276, 6.774)
Log-rank p-value		0.692

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	97.1 (95.0, 99.1)
6 months	99.3 (97.9, 100.0)	97.1 (95.0, 99.1)
9 months	99.3 (97.9, 100.0)	97.1 (95.0, 99.1)
12 months	0.0 (NE, NE)	97.1 (95.0, 99.1)
18 months	0.0 (NE, NE)	97.1 (95.0, 99.1)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	1 (0.7)	8 (2.8)
Number of Subjects Censored, n (%)	144 (99.3)	279 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.098 (1.084)
95% CI		(0.250, 17.576)
Log-rank p-value		0.439

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.6, 100.0)	98.9 (97.6, 100.0)
6 months	99.2 (97.6, 100.0)	94.5 (90.5, 98.5)
9 months	99.2 (97.6, 100.0)	94.5 (90.5, 98.5)
12 months	99.2 (97.6, 100.0)	94.5 (90.5, 98.5)
18 months	NE (NE, NE)	94.5 (90.5, 98.5)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	42 (29.0)	117 (40.8)
Number of Subjects Censored, n (%)	103 (71.0)	170 (59.2)
Time to first TEAE (months)		
25% percentile (95% CI)	1.61 (0.92, 5.82)	1.58 (0.95, 1.84)
Median (95% CI)	5.82 (5.59, NE)	7.85 (5.78, NE)
75% percentile (95% CI)	NE (5.82, NE)	NE (16.79, NE)
Min, Max	0.0, 6.5*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.204 (0.184)
95% CI		(0.839, 1.726)
Log-rank p-value		0.255

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.0 (63.3, 78.7)	61.9 (56.0, 67.7)
6 months	45.6 (15.9, 75.3)	55.1 (48.1, 62.0)
9 months	NE (NE, NE)	49.7 (41.6, 57.8)
12 months	NE (NE, NE)	49.7 (41.6, 57.8)
18 months	NE (NE, NE)	37.3 (15.3, 59.2)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	10 (6.9)	37 (12.9)
Number of Subjects Censored, n (%)	135 (93.1)	250 (87.1)
Time to first TEAE (months)		
25% percentile (95% CI)	5.82 (5.59, NE)	NE (7.85, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (5.82, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.461 (0.364)
95% CI		(0.715, 2.985)
Log-rank p-value		0.243

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.6 (89.1, 98.0)	88.3 (84.4, 92.2)
6 months	65.5 (31.9, 99.1)	85.0 (80.0, 90.0)
9 months	NE (NE, NE)	81.4 (74.6, 88.3)
12 months	NE (NE, NE)	81.4 (74.6, 88.3)
18 months	NE (NE, NE)	81.4 (74.6, 88.3)
Median Follow-up Time (months)	2.83	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	9 (6.2)	33 (11.5)
Number of Subjects Censored, n (%)	136 (93.8)	254 (88.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.419 (0.385)
95% CI		(0.667, 3.019)
Log-rank p-value		0.369

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.3 (90.4, 98.1)	89.7 (86.1, 93.4)
6 months	82.5 (60.6, 100.0)	87.0 (82.2, 91.7)
9 months	NE (NE, NE)	83.7 (77.4, 90.1)
12 months	NE (NE, NE)	83.7 (77.4, 90.1)
18 months	NE (NE, NE)	83.7 (77.4, 90.1)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	8 (5.5)	30 (10.5)
Number of Subjects Censored, n (%)	137 (94.5)	257 (89.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.584 (0.404)
95% CI		(0.717, 3.497)
Log-rank p-value		0.284

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (91.5, 98.6)	90.5 (87.0, 94.0)
6 months	83.2 (61.2, 100.0)	88.6 (84.4, 92.9)
9 months	NE (NE, NE)	85.4 (79.3, 91.5)
12 months	NE (NE, NE)	85.4 (79.3, 91.5)
18 months	NE (NE, NE)	85.4 (79.3, 91.5)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	8 (5.5)	26 (9.1)
Number of Subjects Censored, n (%)	137 (94.5)	261 (90.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.202 (0.412)
95% CI		(0.537, 2.694)
Log-rank p-value		0.777

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (90.6, 98.2)	92.5 (89.3, 95.7)
6 months	94.4 (90.6, 98.2)	88.9 (84.6, 93.3)
9 months	94.4 (90.6, 98.2)	87.5 (82.3, 92.6)
12 months	94.4 (90.6, 98.2)	87.5 (82.3, 92.6)
18 months	NE (NE, NE)	87.5 (82.3, 92.6)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	3 (2.1)	19 (6.6)
Number of Subjects Censored, n (%)	142 (97.9)	268 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.865 (0.630)
95% CI		(0.833, 9.848)
Log-rank p-value		0.078

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (95.9, 100.0)	93.2 (90.1, 96.2)
6 months	94.0 (85.5, 100.0)	92.2 (88.7, 95.8)
9 months	94.0 (85.5, 100.0)	92.2 (88.7, 95.8)
12 months	94.0 (85.5, 100.0)	92.2 (88.7, 95.8)
18 months	NE (NE, NE)	92.2 (88.7, 95.8)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	7 (4.8)	16 (5.6)
Number of Subjects Censored, n (%)	138 (95.2)	271 (94.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.900 (0.464)
95% CI		(0.362, 2.235)
Log-rank p-value		0.837

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.5 (90.5, 98.5)	94.9 (92.3, 97.5)
6 months	94.5 (90.5, 98.5)	92.9 (89.1, 96.7)
9 months	94.5 (90.5, 98.5)	92.9 (89.1, 96.7)
12 months	94.5 (90.5, 98.5)	92.9 (89.1, 96.7)
18 months	NE (NE, NE)	92.9 (89.1, 96.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	2 (1.4)	23 (8.0)
Number of Subjects Censored, n (%)	143 (98.6)	264 (92.0)
Time to first TEAE (months)		
25% percentile (95% CI)	7.43 (7.43, NE)	NE (NE, NE)
Median (95% CI)	7.43 (7.43, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (7.43, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.191 (0.744)
95% CI		(1.208, 22.303)
Log-rank p-value		0.016

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (98.0, 100.0)	92.7 (89.7, 95.8)
6 months	99.3 (98.0, 100.0)	90.5 (86.6, 94.4)
9 months	NE (NE, NE)	90.5 (86.6, 94.4)
12 months	NE (NE, NE)	90.5 (86.6, 94.4)
18 months	NE (NE, NE)	90.5 (86.6, 94.4)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	3 (2.1)	14 (4.9)
Number of Subjects Censored, n (%)	142 (97.9)	273 (95.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.955 (0.645)
95% CI		(0.552, 6.927)
Log-rank p-value		0.282

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (94.9, 100.0)	95.3 (92.7, 97.9)
6 months	97.6 (94.9, 100.0)	94.7 (91.8, 97.6)
9 months	97.6 (94.9, 100.0)	93.5 (89.8, 97.1)
12 months	97.6 (94.9, 100.0)	93.5 (89.8, 97.1)
18 months	NE (NE, NE)	93.5 (89.8, 97.1)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	1 (0.7)	7 (2.4)
Number of Subjects Censored, n (%)	144 (99.3)	280 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.997 (1.115)
95% CI		(0.337, 26.673)
Log-rank p-value		0.312

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	97.5 (95.6, 99.5)
6 months	99.3 (97.9, 100.0)	96.7 (94.2, 99.3)
9 months	99.3 (97.9, 100.0)	96.7 (94.2, 99.3)
12 months	99.3 (97.9, 100.0)	96.7 (94.2, 99.3)
18 months	NE (NE, NE)	96.7 (94.2, 99.3)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	2 (1.4)	4 (1.4)
Number of Subjects Censored, n (%)	143 (98.6)	283 (98.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.915 (0.949)
95% CI		(0.143, 5.878)
Log-rank p-value		0.933

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.6, 100.0)	98.6 (97.1, 100.0)
6 months	98.6 (96.6, 100.0)	98.6 (97.1, 100.0)
9 months	98.6 (96.6, 100.0)	98.6 (97.1, 100.0)
12 months	98.6 (96.6, 100.0)	98.6 (97.1, 100.0)
18 months	NE (NE, NE)	98.6 (97.1, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	37 (25.5)	110 (38.3)
Number of Subjects Censored, n (%)	108 (74.5)	177 (61.7)
Time to first TEAE (months)		
25% percentile (95% CI)	2.53 (0.76, NE)	0.89 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	11.53 (6.41, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.456 (0.192)
95% CI		(0.999, 2.123)
Log-rank p-value		0.056

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.0 (65.4, 80.6)	65.7 (60.2, 71.3)
6 months	73.0 (65.4, 80.6)	59.3 (52.8, 65.8)
9 months	73.0 (65.4, 80.6)	56.9 (49.9, 63.9)
12 months	73.0 (65.4, 80.6)	44.8 (27.1, 62.5)
18 months	NE (NE, NE)	44.8 (27.1, 62.5)
Median Follow-up Time (months)	2.23	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	7 (4.8)	45 (15.7)
Number of Subjects Censored, n (%)	138 (95.2)	242 (84.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.412 (0.407)
95% CI		(1.537, 7.573)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.7 (90.7, 98.6)	84.4 (80.2, 88.7)
6 months	94.7 (90.7, 98.6)	83.9 (79.5, 88.2)
9 months	94.7 (90.7, 98.6)	83.9 (79.5, 88.2)
12 months	94.7 (90.7, 98.6)	83.9 (79.5, 88.2)
18 months	NE (NE, NE)	83.9 (79.5, 88.2)
Median Follow-up Time (months)	2.79	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	14 (9.7)	29 (10.1)
Number of Subjects Censored, n (%)	131 (90.3)	258 (89.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	14.32 (14.32, NE)
Median (95% CI)	NE (NE, NE)	NE (14.32, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.897 (0.334)
95% CI		(0.466, 1.726)
Log-rank p-value		0.771

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.2 (85.4, 95.1)	91.8 (88.6, 95.0)
6 months	90.2 (85.4, 95.1)	88.6 (84.2, 93.0)
9 months	90.2 (85.4, 95.1)	87.4 (82.5, 92.4)
12 months	90.2 (85.4, 95.1)	87.4 (82.5, 92.4)
18 months	NE (NE, NE)	69.9 (39.0, 100.0)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	14 (9.7)	22 (7.7)
Number of Subjects Censored, n (%)	131 (90.3)	265 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.668 (0.355)
95% CI		(0.333, 1.338)
Log-rank p-value		0.218

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.9 (84.9, 95.0)	93.6 (90.8, 96.5)
6 months	89.9 (84.9, 95.0)	92.2 (88.7, 95.6)
9 months	89.9 (84.9, 95.0)	90.9 (86.6, 95.1)
12 months	89.9 (84.9, 95.0)	81.8 (64.5, 99.1)
18 months	NE (NE, NE)	81.8 (64.5, 99.1)
Median Follow-up Time (months)	2.60	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	2 (1.4)	11 (3.8)
Number of Subjects Censored, n (%)	143 (98.6)	276 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.166 (0.793)
95% CI		(0.669, 14.994)
Log-rank p-value		0.151

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.7, 100.0)	96.0 (93.7, 98.3)
6 months	98.6 (96.7, 100.0)	96.0 (93.7, 98.3)
9 months	98.6 (96.7, 100.0)	96.0 (93.7, 98.3)
12 months	98.6 (96.7, 100.0)	96.0 (93.7, 98.3)
18 months	NE (NE, NE)	96.0 (93.7, 98.3)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	1 (0.7)	8 (2.8)
Number of Subjects Censored, n (%)	144 (99.3)	279 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.426 (1.125)
95% CI		(0.377, 31.103)
Log-rank p-value		0.222

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	98.2 (96.7, 99.8)
6 months	99.3 (97.9, 100.0)	97.3 (94.9, 99.7)
9 months	99.3 (97.9, 100.0)	94.2 (89.4, 99.0)
12 months	99.3 (97.9, 100.0)	94.2 (89.4, 99.0)
18 months	NE (NE, NE)	94.2 (89.4, 99.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Vascular disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	23 (15.9)	113 (39.4)
Number of Subjects Censored, n (%)	122 (84.1)	174 (60.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.89 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	NE (6.44, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.654 (0.230)
95% CI		(1.690, 4.169)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Vascular disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.3 (77.1, 89.6)	61.0 (55.1, 66.8)
6 months	83.3 (77.1, 89.6)	57.8 (51.5, 64.2)
9 months	NE (NE, NE)	54.6 (47.2, 62.1)
12 months	NE (NE, NE)	54.6 (47.2, 62.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.53	2.69

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	13 (9.0)	104 (36.2)
Number of Subjects Censored, n (%)	132 (91.0)	183 (63.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.99 (0.69, 1.94)
Median (95% CI)	NE (NE, NE)	NE (7.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.359 (0.296)
95% CI		(2.439, 7.790)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.6 (85.7, 95.5)	64.3 (58.6, 70.1)
6 months	90.6 (85.7, 95.5)	62.2 (56.2, 68.3)
9 months	NE (NE, NE)	57.3 (49.5, 65.0)
12 months	NE (NE, NE)	57.3 (49.5, 65.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	22 (15.2)	93 (32.4)
Number of Subjects Censored, n (%)	123 (84.8)	194 (67.6)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (5.59, NE)	1.64 (0.99, 2.99)
Median (95% CI)	NE (5.59, NE)	NE (8.64, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.003 (0.242)
95% CI		(1.247, 3.216)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.9 (79.0, 90.9)	69.6 (64.2, 75.1)
6 months	70.8 (45.0, 96.6)	65.2 (58.8, 71.6)
9 months	NE (NE, NE)	59.1 (50.2, 68.1)
12 months	NE (NE, NE)	55.4 (44.5, 66.4)
18 months	NE (NE, NE)	55.4 (44.5, 66.4)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	8 (5.5)	30 (10.5)
Number of Subjects Censored, n (%)	137 (94.5)	257 (89.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.455 (0.405)
95% CI		(0.658, 3.219)
Log-rank p-value		0.343

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.2 (90.3, 98.1)	91.0 (87.6, 94.5)
6 months	94.2 (90.3, 98.1)	87.2 (82.4, 91.9)
9 months	94.2 (90.3, 98.1)	85.9 (80.7, 91.2)
12 months	94.2 (90.3, 98.1)	85.9 (80.7, 91.2)
18 months	NE (NE, NE)	85.9 (80.7, 91.2)
Median Follow-up Time (months)	2.79	3.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	5 (3.4)	24 (8.4)
Number of Subjects Censored, n (%)	140 (96.6)	263 (91.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.072 (0.504)
95% CI		(0.772, 5.558)
Log-rank p-value		0.144

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (94.2, 99.9)	92.3 (89.2, 95.5)
6 months	84.9 (62.6, 100.0)	91.6 (88.2, 95.1)
9 months	NE (NE, NE)	88.2 (82.5, 93.9)
12 months	NE (NE, NE)	88.2 (82.5, 93.9)
18 months	NE (NE, NE)	88.2 (82.5, 93.9)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	2 (1.4)	22 (7.7)
Number of Subjects Censored, n (%)	143 (98.6)	265 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.485 (0.754)
95% CI		(1.481, 28.402)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.2, 100.0)	92.4 (89.3, 95.6)
6 months	98.4 (96.2, 100.0)	91.4 (87.8, 95.1)
9 months	98.4 (96.2, 100.0)	91.4 (87.8, 95.1)
12 months	98.4 (96.2, 100.0)	91.4 (87.8, 95.1)
18 months	NE (NE, NE)	91.4 (87.8, 95.1)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	3 (2.1)	8 (2.8)
Number of Subjects Censored, n (%)	142 (97.9)	279 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.138 (0.685)
95% CI		(0.297, 4.360)
Log-rank p-value		0.852

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.4, 100.0)	97.5 (95.6, 99.3)
6 months	97.8 (95.4, 100.0)	96.3 (93.4, 99.2)
9 months	97.8 (95.4, 100.0)	96.3 (93.4, 99.2)
12 months	97.8 (95.4, 100.0)	96.3 (93.4, 99.2)
18 months	NE (NE, NE)	96.3 (93.4, 99.2)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	1 (0.7)	10 (3.5)
Number of Subjects Censored, n (%)	144 (99.3)	277 (96.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.926 (1.076)
95% CI		(0.355, 24.097)
Log-rank p-value		0.243

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	97.8 (96.1, 99.6)
6 months	99.3 (97.9, 100.0)	96.8 (94.1, 99.5)
9 months	99.3 (97.9, 100.0)	90.2 (82.3, 98.1)
12 months	99.3 (97.9, 100.0)	90.2 (82.3, 98.1)
18 months	NE (NE, NE)	90.2 (82.3, 98.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	0	8 (2.8)
Number of Subjects Censored, n (%)	145 (100.0)	279 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.070

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.0 (95.0, 99.1)
6 months	100.0 (100.0, 100.0)	97.0 (95.0, 99.1)
9 months	100.0 (100.0, 100.0)	97.0 (95.0, 99.1)
12 months	100.0 (100.0, 100.0)	97.0 (95.0, 99.1)
18 months	NE (NE, NE)	97.0 (95.0, 99.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	17 (11.7)	102 (35.5)
Number of Subjects Censored, n (%)	128 (88.3)	185 (64.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	1.48 (0.72, 1.71)
Median (95% CI)	NE (NE, NE)	NE (7.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.980 (0.264)
95% CI		(1.777, 4.999)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.6 (83.4, 93.9)	66.5 (60.9, 72.1)
6 months	84.0 (73.8, 94.2)	61.1 (54.6, 67.6)
9 months	84.0 (73.8, 94.2)	57.5 (49.7, 65.4)
12 months	84.0 (73.8, 94.2)	57.5 (49.7, 65.4)
18 months	NE (NE, NE)	57.5 (49.7, 65.4)
Median Follow-up Time (months)	2.69	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	3 (2.1)	60 (20.9)
Number of Subjects Censored, n (%)	142 (97.9)	227 (79.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	7.39 (3.58, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		9.317 (0.593)
95% CI		(2.916, 29.771)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.9 (95.6, 100.0)	81.5 (76.9, 86.0)
6 months	97.9 (95.6, 100.0)	75.8 (69.9, 81.8)
9 months	97.9 (95.6, 100.0)	73.7 (66.7, 80.8)
12 months	97.9 (95.6, 100.0)	73.7 (66.7, 80.8)
18 months	NE (NE, NE)	73.7 (66.7, 80.8)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	4 (2.8)	11 (3.8)
Number of Subjects Censored, n (%)	141 (97.2)	276 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.162 (0.594)
95% CI		(0.362, 3.723)
Log-rank p-value		0.835

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (94.5, 99.9)	95.9 (93.5, 98.3)
6 months	97.2 (94.5, 99.9)	95.9 (93.5, 98.3)
9 months	97.2 (94.5, 99.9)	95.9 (93.5, 98.3)
12 months	97.2 (94.5, 99.9)	95.9 (93.5, 98.3)
18 months	NE (NE, NE)	95.9 (93.5, 98.3)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	3 (2.1)	8 (2.8)
Number of Subjects Censored, n (%)	142 (97.9)	279 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.085 (0.694)
95% CI		(0.278, 4.230)
Log-rank p-value		0.966

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.4, 100.0)	97.1 (95.1, 99.1)
6 months	94.2 (85.8, 100.0)	97.1 (95.1, 99.1)
9 months	94.2 (85.8, 100.0)	97.1 (95.1, 99.1)
12 months	94.2 (85.8, 100.0)	97.1 (95.1, 99.1)
18 months	NE (NE, NE)	97.1 (95.1, 99.1)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Nervous system disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	27 (18.6)	75 (26.1)
Number of Subjects Censored, n (%)	118 (81.4)	212 (73.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.87, NE)	4.14 (1.84, 6.21)
Median (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.182 (0.228)
95% CI		(0.755, 1.849)
Log-rank p-value		0.478

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Nervous system disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.0 (73.1, 86.8)	77.3 (72.4, 82.3)
6 months	80.0 (73.1, 86.8)	71.1 (64.9, 77.3)
9 months	80.0 (73.1, 86.8)	68.7 (61.8, 75.5)
12 months	80.0 (73.1, 86.8)	63.4 (51.6, 75.2)
18 months	NE (NE, NE)	63.4 (51.6, 75.2)
Median Follow-up Time (months)	2.33	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	7 (4.8)	29 (10.1)
Number of Subjects Censored, n (%)	138 (95.2)	258 (89.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
Median (95% CI)	NE (NE, NE)	NE (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.794 (0.426)
95% CI		(0.778, 4.136)
Log-rank p-value		0.166

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.3 (90.2, 98.5)	91.5 (88.2, 94.7)
6 months	94.3 (90.2, 98.5)	89.8 (85.8, 93.7)
9 months	94.3 (90.2, 98.5)	87.2 (82.1, 92.4)
12 months	94.3 (90.2, 98.5)	87.2 (82.1, 92.4)
18 months	NE (NE, NE)	87.2 (82.1, 92.4)
Median Follow-up Time (months)	2.79	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	6 (4.1)	6 (2.1)
Number of Subjects Censored, n (%)	139 (95.9)	281 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.464 (0.579)
95% CI		(0.149, 1.442)
Log-rank p-value		0.164

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.8 (92.5, 99.1)	97.8 (96.0, 99.5)
6 months	95.8 (92.5, 99.1)	97.8 (96.0, 99.5)
9 months	95.8 (92.5, 99.1)	97.8 (96.0, 99.5)
12 months	95.8 (92.5, 99.1)	97.8 (96.0, 99.5)
18 months	NE (NE, NE)	97.8 (96.0, 99.5)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	3 (2.1)	10 (3.5)
Number of Subjects Censored, n (%)	142 (97.9)	277 (96.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.631 (0.659)
95% CI		(0.448, 5.933)
Log-rank p-value		0.448

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.3, 100.0)	96.4 (94.2, 98.6)
6 months	97.8 (95.3, 100.0)	96.4 (94.2, 98.6)
9 months	97.8 (95.3, 100.0)	96.4 (94.2, 98.6)
12 months	97.8 (95.3, 100.0)	96.4 (94.2, 98.6)
18 months	NE (NE, NE)	96.4 (94.2, 98.6)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	17 (11.7)	70 (24.4)
Number of Subjects Censored, n (%)	128 (88.3)	217 (75.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	4.57 (2.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.929 (0.279)
95% CI		(1.117, 3.332)
Log-rank p-value		0.026

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.7 (81.9, 93.5)	77.0 (72.0, 82.1)
6 months	83.3 (73.3, 93.4)	72.3 (66.3, 78.4)
9 months	83.3 (73.3, 93.4)	69.3 (62.2, 76.4)
12 months	83.3 (73.3, 93.4)	69.3 (62.2, 76.4)
18 months	NE (NE, NE)	69.3 (62.2, 76.4)
Median Follow-up Time (months)	2.76	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	6 (4.1)	53 (18.5)
Number of Subjects Censored, n (%)	139 (95.9)	234 (81.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.75, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.846 (0.449)
95% CI		(2.009, 11.690)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.8 (92.5, 99.1)	81.3 (76.5, 86.0)
6 months	95.8 (92.5, 99.1)	79.2 (74.0, 84.4)
9 months	95.8 (92.5, 99.1)	79.2 (74.0, 84.4)
12 months	95.8 (92.5, 99.1)	79.2 (74.0, 84.4)
18 months	NE (NE, NE)	79.2 (74.0, 84.4)
Median Follow-up Time (months)	2.79	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	2 (1.4)	4 (1.4)
Number of Subjects Censored, n (%)	143 (98.6)	283 (98.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.880 (0.874)
95% CI		(0.159, 4.877)
Log-rank p-value		0.915

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.7, 100.0)	98.6 (97.2, 100.0)
6 months	98.6 (96.7, 100.0)	98.6 (97.2, 100.0)
9 months	98.6 (96.7, 100.0)	98.6 (97.2, 100.0)
12 months	98.6 (96.7, 100.0)	98.6 (97.2, 100.0)
18 months	NE (NE, NE)	98.6 (97.2, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Infections and infestations**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	16 (11.0)	57 (19.9)
Number of Subjects Censored, n (%)	129 (89.0)	230 (80.1)
Time to first TEAE (months)		
25% percentile (95% CI)	5.78 (4.34, NE)	6.37 (4.63, 17.48)
Median (95% CI)	NE (5.78, NE)	17.48 (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.48, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.305 (0.296)
95% CI		(0.730, 2.333)
Log-rank p-value		0.363

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Infections and infestations**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (85.1, 95.0)	85.2 (81.0, 89.5)
6 months	67.2 (36.2, 98.3)	76.0 (69.4, 82.6)
9 months	67.2 (36.2, 98.3)	69.4 (60.7, 78.1)
12 months	67.2 (36.2, 98.3)	62.5 (47.4, 77.6)
18 months	NE (NE, NE)	46.8 (18.0, 75.7)
Median Follow-up Time (months)	2.79	3.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	5 (3.4)	11 (3.8)
Number of Subjects Censored, n (%)	140 (96.6)	276 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.714 (0.612)
95% CI		(0.215, 2.369)
Log-rank p-value		0.577

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (94.5, 99.9)	97.5 (95.7, 99.3)
6 months	91.5 (80.3, 100.0)	94.6 (90.8, 98.3)
9 months	91.5 (80.3, 100.0)	93.3 (88.8, 97.8)
12 months	91.5 (80.3, 100.0)	93.3 (88.8, 97.8)
18 months	NE (NE, NE)	93.3 (88.8, 97.8)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	1 (0.7)	9 (3.1)
Number of Subjects Censored, n (%)	144 (99.3)	278 (96.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (11.56, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.086 (1.073)
95% CI		(0.255, 17.097)
Log-rank p-value		0.510

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.4 (96.8, 100.0)
6 months	94.1 (82.9, 100.0)	96.3 (93.5, 99.1)
9 months	94.1 (82.9, 100.0)	94.8 (90.8, 98.8)
12 months	94.1 (82.9, 100.0)	86.2 (69.7, 100.0)
18 months	NE (NE, NE)	86.2 (69.7, 100.0)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	1 (0.7)	8 (2.8)
Number of Subjects Censored, n (%)	144 (99.3)	279 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.741 (1.086)
95% CI		(0.445, 31.431)
Log-rank p-value		0.246

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	97.2 (95.2, 99.3)
6 months	99.3 (97.9, 100.0)	96.2 (93.3, 99.1)
9 months	99.3 (97.9, 100.0)	96.2 (93.3, 99.1)
12 months	99.3 (97.9, 100.0)	96.2 (93.3, 99.1)
18 months	NE (NE, NE)	96.2 (93.3, 99.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	22 (15.2)	41 (14.3)
Number of Subjects Censored, n (%)	123 (84.8)	246 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.77, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.809 (0.271)
95% CI		(0.476, 1.376)
Log-rank p-value		0.458

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.4 (77.0, 89.8)	86.1 (81.9, 90.3)
6 months	83.4 (77.0, 89.8)	83.3 (78.1, 88.5)
9 months	83.4 (77.0, 89.8)	81.6 (75.6, 87.6)
12 months	83.4 (77.0, 89.8)	81.6 (75.6, 87.6)
18 months	NE (NE, NE)	81.6 (75.6, 87.6)
Median Follow-up Time (months)	2.60	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	15 (10.3)	23 (8.0)
Number of Subjects Censored, n (%)	130 (89.7)	264 (92.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	17.74 (17.74, NE)
Median (95% CI)	NE (NE, NE)	NE (17.74, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.74, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.611 (0.348)
95% CI		(0.309, 1.207)
Log-rank p-value		0.163

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.4 (82.8, 94.0)	92.8 (89.6, 95.9)
6 months	88.4 (82.8, 94.0)	90.1 (85.8, 94.4)
9 months	88.4 (82.8, 94.0)	90.1 (85.8, 94.4)
12 months	88.4 (82.8, 94.0)	90.1 (85.8, 94.4)
18 months	NE (NE, NE)	60.1 (11.9, 100.0)
Median Follow-up Time (months)	2.69	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	1 (0.7)	19 (6.6)
Number of Subjects Censored, n (%)	144 (99.3)	268 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		9.408 (1.027)
95% CI		(1.258, 70.365)
Log-rank p-value		0.008

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	92.9 (89.8, 96.0)
6 months	99.3 (97.9, 100.0)	92.9 (89.8, 96.0)
9 months	99.3 (97.9, 100.0)	92.9 (89.8, 96.0)
12 months	99.3 (97.9, 100.0)	92.9 (89.8, 96.0)
18 months	NE (NE, NE)	92.9 (89.8, 96.0)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Endocrine disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	1 (0.7)	62 (21.6)
Number of Subjects Censored, n (%)	144 (99.3)	225 (78.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.52 (3.81, 6.47)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6, 12.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		28.373 (1.027)
95% CI		(3.790, 212.416)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Endocrine disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	84.2 (79.8, 88.6)
6 months	99.3 (97.9, 100.0)	68.4 (60.7, 76.2)
9 months	99.3 (97.9, 100.0)	65.3 (56.7, 73.8)
12 months	99.3 (97.9, 100.0)	65.3 (56.7, 73.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	1 (0.7)	60 (20.9)
Number of Subjects Censored, n (%)	144 (99.3)	227 (79.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.59 (3.84, 6.90)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6, 12.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		26.871 (1.027)
95% CI		(3.587, 201.321)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	85.0 (80.7, 89.3)
6 months	99.3 (97.9, 100.0)	70.1 (62.5, 77.7)
9 months	99.3 (97.9, 100.0)	64.9 (55.7, 74.0)
12 months	99.3 (97.9, 100.0)	64.9 (55.7, 74.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	10 (6.9)	34 (11.8)
Number of Subjects Censored, n (%)	135 (93.1)	253 (88.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.409 (0.370)
95% CI		(0.682, 2.912)
Log-rank p-value		0.293

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.7 (88.3, 97.1)	89.9 (86.2, 93.5)
6 months	92.7 (88.3, 97.1)	85.0 (79.9, 90.2)
9 months	92.7 (88.3, 97.1)	83.6 (77.8, 89.4)
12 months	92.7 (88.3, 97.1)	83.6 (77.8, 89.4)
18 months	NE (NE, NE)	83.6 (77.8, 89.4)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	7 (4.8)	13 (4.5)
Number of Subjects Censored, n (%)	138 (95.2)	274 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.628 (0.487)
95% CI		(0.242, 1.630)
Log-rank p-value		0.330

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (91.5, 98.6)	96.1 (93.7, 98.5)
6 months	95.1 (91.5, 98.6)	94.5 (91.2, 97.7)
9 months	95.1 (91.5, 98.6)	92.9 (88.5, 97.3)
12 months	95.1 (91.5, 98.6)	92.9 (88.5, 97.3)
18 months	NE (NE, NE)	92.9 (88.5, 97.3)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	0	5 (1.7)
Number of Subjects Censored, n (%)	145 (100.0)	282 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.096

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.2 (96.5, 99.8)
6 months	100.0 (100.0, 100.0)	98.2 (96.5, 99.8)
9 months	100.0 (100.0, 100.0)	98.2 (96.5, 99.8)
12 months	100.0 (100.0, 100.0)	98.2 (96.5, 99.8)
18 months	NE (NE, NE)	98.2 (96.5, 99.8)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	1 (0.7)	11 (3.8)
Number of Subjects Censored, n (%)	144 (99.3)	276 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.698 (1.085)
95% CI		(0.799, 56.184)
Log-rank p-value		0.028

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.1, 100.0)	96.6 (94.5, 98.8)
6 months	99.0 (97.1, 100.0)	95.0 (91.9, 98.1)
9 months	99.0 (97.1, 100.0)	95.0 (91.9, 98.1)
12 months	99.0 (97.1, 100.0)	95.0 (91.9, 98.1)
18 months	NE (NE, NE)	95.0 (91.9, 98.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	12 (8.3)	29 (10.1)
Number of Subjects Censored, n (%)	133 (91.7)	258 (89.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.66, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.839 (0.353)
95% CI		(0.420, 1.676)
Log-rank p-value		0.710

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (86.6, 96.0)	91.9 (88.5, 95.2)
6 months	91.3 (86.6, 96.0)	87.2 (82.3, 92.1)
9 months	91.3 (86.6, 96.0)	85.3 (79.2, 91.4)
12 months	91.3 (86.6, 96.0)	81.7 (72.7, 90.7)
18 months	NE (NE, NE)	81.7 (72.7, 90.7)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	2 (1.4)	12 (4.2)
Number of Subjects Censored, n (%)	143 (98.6)	275 (95.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.193 (0.772)
95% CI		(0.483, 9.953)
Log-rank p-value		0.315

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.3, 100.0)	96.0 (93.5, 98.5)
6 months	98.4 (96.3, 100.0)	95.3 (92.5, 98.1)
9 months	98.4 (96.3, 100.0)	95.3 (92.5, 98.1)
12 months	98.4 (96.3, 100.0)	91.3 (83.2, 99.4)
18 months	NE (NE, NE)	91.3 (83.2, 99.4)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3H
Summary of Time to Onset of TEAE by SOC/PT by RAS Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Mutant

Statistics	Placebo + BSC N=145	Fruquintinib + BSC N=287
Number of Subjects with Events, n (%)	1 (0.7)	8 (2.8)
Number of Subjects Censored, n (%)	144 (99.3)	279 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.014 (1.087)
95% CI		(0.239, 16.958)
Log-rank p-value		0.454

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	114 (57.9)	278 (70.0)
Number of Subjects Censored, n (%)	83 (42.1)	119 (30.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.46, 0.69)	0.43 (0.30, 0.62)
Median (95% CI)	1.87 (1.28, 2.76)	1.08 (0.92, 1.61)
75% percentile (95% CI)	NE (4.70, NE)	5.98 (4.47, NE)
Min, Max	0.0, 6.8*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.203 (0.112)
95% CI		(0.965, 1.500)
Log-rank p-value		0.132

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	41.7 (34.4, 48.9)	36.9 (32.1, 41.7)
6 months	31.6 (20.4, 42.8)	24.6 (19.5, 29.7)
9 months	NE (NE, NE)	20.1 (14.3, 25.9)
12 months	NE (NE, NE)	20.1 (14.3, 25.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.61	1.05

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	46 (23.4)	139 (35.0)
Number of Subjects Censored, n (%)	151 (76.6)	258 (65.0)
Time to first TEAE (months)		
25% percentile (95% CI)	3.22 (1.35, NE)	1.18 (0.89, 1.68)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.403 (0.171)
95% CI		(1.003, 1.962)
Log-rank p-value		0.053

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.1 (69.8, 82.4)	67.0 (62.3, 71.7)
6 months	68.5 (56.3, 80.7)	62.4 (57.2, 67.7)
9 months	NE (NE, NE)	59.4 (52.8, 66.1)
12 months	NE (NE, NE)	59.4 (52.8, 66.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.40	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	30 (15.2)	80 (20.2)
Number of Subjects Censored, n (%)	167 (84.8)	317 (79.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.71, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.225 (0.215)
95% CI		(0.803, 1.868)
Log-rank p-value		0.378

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.4 (77.9, 88.9)	81.1 (77.1, 85.0)
6 months	83.4 (77.9, 88.9)	78.3 (73.9, 82.7)
9 months	NE (NE, NE)	77.0 (72.0, 82.0)
12 months	NE (NE, NE)	77.0 (72.0, 82.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	21 (10.7)	45 (11.3)
Number of Subjects Censored, n (%)	176 (89.3)	352 (88.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.70, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.866 (0.270)
95% CI		(0.510, 1.470)
Log-rank p-value		0.526

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.6 (83.8, 93.4)	90.6 (87.7, 93.6)
6 months	83.1 (71.6, 94.5)	87.6 (83.8, 91.3)
9 months	NE (NE, NE)	85.9 (81.5, 90.2)
12 months	NE (NE, NE)	80.1 (68.6, 91.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	6 (3.0)	51 (12.8)
Number of Subjects Censored, n (%)	191 (97.0)	346 (87.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
Median (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.24, NE)
Min, Max	0.1, 8.4*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.924 (0.434)
95% CI		(1.677, 9.182)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.7 (94.1, 99.3)	88.5 (85.3, 91.6)
6 months	96.7 (94.1, 99.3)	87.0 (83.4, 90.5)
9 months	NE (NE, NE)	84.3 (79.4, 89.3)
12 months	NE (NE, NE)	84.3 (79.4, 89.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.45

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	26 (13.2)	20 (5.0)
Number of Subjects Censored, n (%)	171 (86.8)	377 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.285 (0.303)
95% CI		(0.157, 0.516)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.1 (80.8, 91.3)	96.2 (94.3, 98.2)
6 months	81.8 (74.2, 89.5)	93.4 (90.4, 96.3)
9 months	NE (NE, NE)	93.4 (90.4, 96.3)
12 months	NE (NE, NE)	93.4 (90.4, 96.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	16 (8.1)	17 (4.3)
Number of Subjects Censored, n (%)	181 (91.9)	380 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.427 (0.360)
95% CI		(0.211, 0.865)
Log-rank p-value		0.015

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (87.2, 95.4)	96.0 (94.0, 98.0)
6 months	91.3 (87.2, 95.4)	96.0 (94.0, 98.0)
9 months	NE (NE, NE)	93.5 (88.2, 98.7)
12 months	NE (NE, NE)	89.9 (81.3, 98.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	4 (2.0)	14 (3.5)
Number of Subjects Censored, n (%)	193 (98.0)	383 (96.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.82, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.3, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.974 (0.595)
95% CI		(0.303, 3.128)
Log-rank p-value		0.890

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (95.5, 100.0)	98.1 (96.8, 99.5)
6 months	97.7 (95.5, 100.0)	96.2 (93.8, 98.5)
9 months	NE (NE, NE)	94.7 (90.9, 98.4)
12 months	NE (NE, NE)	87.8 (77.9, 97.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	4 (2.0)	11 (2.8)
Number of Subjects Censored, n (%)	193 (98.0)	386 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.4, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.924 (0.597)
95% CI		(0.286, 2.979)
Log-rank p-value		0.832

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (94.7, 100.0)	97.8 (96.2, 99.3)
6 months	97.4 (94.7, 100.0)	96.7 (94.6, 98.8)
9 months	NE (NE, NE)	95.2 (91.6, 98.8)
12 months	NE (NE, NE)	95.2 (91.6, 98.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	2 (1.0)	9 (2.3)
Number of Subjects Censored, n (%)	195 (99.0)	388 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.616 (0.808)
95% CI		(0.332, 7.869)
Log-rank p-value		0.519

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.6, 100.0)	98.5 (97.3, 99.7)
6 months	99.0 (97.6, 100.0)	97.2 (94.9, 99.4)
9 months	NE (NE, NE)	94.8 (89.9, 99.8)
12 months	NE (NE, NE)	94.8 (89.9, 99.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	112 (56.9)	266 (67.0)
Number of Subjects Censored, n (%)	85 (43.1)	131 (33.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.49 (0.30, 0.69)	0.49 (0.43, 0.69)
Median (95% CI)	1.61 (1.22, 2.79)	1.54 (1.05, 1.91)
75% percentile (95% CI)	5.36 (4.34, NE)	6.70 (4.90, 10.12)
Min, Max	0.0, 5.6*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.037 (0.115)
95% CI		(0.828, 1.299)
Log-rank p-value		0.742

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	40.5 (32.7, 48.3)	39.5 (34.5, 44.4)
6 months	NE (NE, NE)	25.6 (19.9, 31.3)
9 months	NE (NE, NE)	19.1 (12.5, 25.7)
12 months	NE (NE, NE)	15.3 (6.8, 23.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.31	1.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	21 (10.7)	99 (24.9)
Number of Subjects Censored, n (%)	176 (89.3)	298 (75.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.96 (2.37, 6.70)
Median (95% CI)	NE (NE, NE)	NE (10.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.068 (0.243)
95% CI		(1.285, 3.326)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.0 (84.6, 93.5)	78.1 (73.9, 82.3)
6 months	89.0 (84.6, 93.5)	71.3 (65.8, 76.9)
9 months	NE (NE, NE)	67.8 (61.3, 74.4)
12 months	NE (NE, NE)	61.7 (48.7, 74.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	38 (19.3)	71 (17.9)
Number of Subjects Censored, n (%)	159 (80.7)	326 (82.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.91, NE)	9.20 (5.55, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.717 (0.207)
95% CI		(0.478, 1.076)
Log-rank p-value		0.116

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.1 (74.3, 86.0)	84.2 (80.4, 88.0)
6 months	76.3 (67.2, 85.5)	78.5 (73.5, 83.5)
9 months	NE (NE, NE)	76.0 (70.0, 82.0)
12 months	NE (NE, NE)	73.4 (65.7, 81.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	3.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	33 (16.8)	69 (17.4)
Number of Subjects Censored, n (%)	164 (83.2)	328 (82.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.92, NE)	7.98 (5.52, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.744 (0.220)
95% CI		(0.483, 1.144)
Log-rank p-value		0.230

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.4 (75.1, 87.6)	85.9 (82.3, 89.6)
6 months	77.7 (68.4, 86.9)	80.1 (75.3, 84.9)
9 months	NE (NE, NE)	74.5 (67.8, 81.2)
12 months	NE (NE, NE)	68.0 (57.4, 78.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	17 (8.6)	68 (17.1)
Number of Subjects Censored, n (%)	180 (91.4)	329 (82.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	9.33 (5.62, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.464 (0.275)
95% CI		(0.853, 2.511)
Log-rank p-value		0.170

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (84.7, 95.3)	85.3 (81.6, 89.0)
6 months	88.1 (81.6, 94.5)	79.3 (74.3, 84.3)
9 months	NE (NE, NE)	75.7 (69.4, 81.9)
12 months	NE (NE, NE)	72.7 (64.5, 80.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	26 (13.2)	55 (13.9)
Number of Subjects Censored, n (%)	171 (86.8)	342 (86.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.36, NE)	10.18 (7.10, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.737 (0.246)
95% CI		(0.455, 1.194)
Log-rank p-value		0.222

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.8 (81.9, 91.8)	89.6 (86.5, 92.7)
6 months	79.2 (67.3, 91.0)	83.9 (79.3, 88.4)
9 months	NE (NE, NE)	79.7 (73.7, 85.6)
12 months	NE (NE, NE)	73.7 (64.0, 83.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	7 (3.6)	63 (15.9)
Number of Subjects Censored, n (%)	190 (96.4)	334 (84.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.98, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.942 (0.429)
95% CI		(2.134, 11.447)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.1 (93.3, 98.9)	85.6 (82.2, 89.1)
6 months	96.1 (93.3, 98.9)	83.1 (79.0, 87.1)
9 months	NE (NE, NE)	80.5 (75.2, 85.8)
12 months	NE (NE, NE)	80.5 (75.2, 85.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	7 (3.6)	28 (7.1)
Number of Subjects Censored, n (%)	190 (96.4)	369 (92.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.641 (0.428)
95% CI		(0.709, 3.796)
Log-rank p-value		0.272

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.2 (93.5, 99.0)	94.2 (91.8, 96.6)
6 months	96.2 (93.5, 99.0)	91.6 (88.3, 94.8)
9 months	NE (NE, NE)	90.0 (85.6, 94.4)
12 months	NE (NE, NE)	90.0 (85.6, 94.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	4 (2.0)	16 (4.0)
Number of Subjects Censored, n (%)	193 (98.0)	381 (96.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.661 (0.567)
95% CI		(0.546, 5.049)
Log-rank p-value		0.359

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.7, 99.9)	96.7 (94.9, 98.5)
6 months	97.8 (95.7, 99.9)	95.4 (92.9, 97.9)
9 months	NE (NE, NE)	93.9 (90.1, 97.7)
12 months	NE (NE, NE)	93.9 (90.1, 97.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	4 (2.0)	8 (2.0)
Number of Subjects Censored, n (%)	193 (98.0)	389 (98.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.849 (0.614)
95% CI		(0.255, 2.830)
Log-rank p-value		0.842

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (95.3, 100.0)	97.8 (96.3, 99.3)
6 months	97.6 (95.3, 100.0)	97.8 (96.3, 99.3)
9 months	NE (NE, NE)	97.8 (96.3, 99.3)
12 months	NE (NE, NE)	97.8 (96.3, 99.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	9 (4.6)	2 (0.5)
Number of Subjects Censored, n (%)	188 (95.4)	395 (99.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.071 (0.831)
95% CI		(0.014, 0.363)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (91.7, 98.2)	99.7 (99.2, 100.0)
6 months	94.9 (91.7, 98.2)	98.9 (97.2, 100.0)
9 months	NE (NE, NE)	98.9 (97.2, 100.0)
12 months	NE (NE, NE)	98.9 (97.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	0	13 (3.3)
Number of Subjects Censored, n (%)	197 (100.0)	384 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.018

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.8 (95.0, 98.6)
6 months	100.0 (100.0, 100.0)	96.8 (95.0, 98.6)
9 months	NE (NE, NE)	95.1 (91.5, 98.8)
12 months	NE (NE, NE)	95.1 (91.5, 98.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	54 (27.4)	176 (44.3)
Number of Subjects Censored, n (%)	143 (72.6)	221 (55.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.92, NE)	1.08 (0.89, 1.61)
Median (95% CI)	NE (NE, NE)	6.28 (4.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.469 (0.158)
95% CI		(1.078, 2.004)
Log-rank p-value		0.018

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.1 (65.6, 78.7)	58.5 (53.4, 63.5)
6 months	66.3 (56.3, 76.3)	52.8 (47.3, 58.3)
9 months	NE (NE, NE)	47.8 (41.5, 54.2)
12 months	NE (NE, NE)	45.3 (37.6, 53.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.40	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	38 (19.3)	112 (28.2)
Number of Subjects Censored, n (%)	159 (80.7)	285 (71.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.91, NE)	2.76 (1.84, 4.63)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.323 (0.191)
95% CI		(0.909, 1.925)
Log-rank p-value		0.166

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.1 (74.3, 85.9)	72.6 (68.0, 77.2)
6 months	76.6 (68.0, 85.3)	69.1 (64.0, 74.2)
9 months	NE (NE, NE)	67.5 (62.1, 72.9)
12 months	NE (NE, NE)	64.9 (57.7, 72.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	3 (1.5)	27 (6.8)
Number of Subjects Censored, n (%)	194 (98.5)	370 (93.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.757 (0.611)
95% CI		(1.134, 12.443)
Log-rank p-value		0.018

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.7, 100.0)	93.1 (90.4, 95.7)
6 months	98.5 (96.7, 100.0)	92.6 (89.8, 95.4)
9 months	NE (NE, NE)	91.1 (87.1, 95.1)
12 months	NE (NE, NE)	91.1 (87.1, 95.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	3 (1.5)	18 (4.5)
Number of Subjects Censored, n (%)	194 (98.5)	379 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.177 (0.632)
95% CI		(0.631, 7.511)
Log-rank p-value		0.189

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.6, 100.0)	96.3 (94.3, 98.2)
6 months	96.8 (92.3, 100.0)	93.9 (90.9, 96.9)
9 months	NE (NE, NE)	93.9 (90.9, 96.9)
12 months	NE (NE, NE)	93.9 (90.9, 96.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	4 (2.0)	12 (3.0)
Number of Subjects Censored, n (%)	193 (98.0)	385 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.6*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.341 (0.579)
95% CI		(0.431, 4.167)
Log-rank p-value		0.643

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (95.4, 100.0)	96.8 (95.0, 98.6)
6 months	97.7 (95.4, 100.0)	96.8 (95.0, 98.6)
9 months	NE (NE, NE)	96.8 (95.0, 98.6)
12 months	NE (NE, NE)	96.8 (95.0, 98.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	2 (1.0)	15 (3.8)
Number of Subjects Censored, n (%)	195 (99.0)	382 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.3, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.251 (0.759)
95% CI		(0.735, 14.381)
Log-rank p-value		0.100

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.5, 100.0)	96.5 (94.6, 98.4)
6 months	99.0 (97.5, 100.0)	95.8 (93.4, 98.1)
9 months	NE (NE, NE)	94.4 (90.8, 97.9)
12 months	NE (NE, NE)	94.4 (90.8, 97.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	0	13 (3.3)
Number of Subjects Censored, n (%)	197 (100.0)	384 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.021

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.1 (95.4, 98.8)
6 months	100.0 (100.0, 100.0)	96.1 (93.9, 98.3)
9 months	NE (NE, NE)	96.1 (93.9, 98.3)
12 months	NE (NE, NE)	96.1 (93.9, 98.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	2 (1.0)	12 (3.0)
Number of Subjects Censored, n (%)	195 (99.0)	385 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.342 (0.769)
95% CI		(0.519, 10.576)
Log-rank p-value		0.241

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.2, 100.0)	97.0 (95.2, 98.8)
6 months	98.4 (96.2, 100.0)	97.0 (95.2, 98.8)
9 months	NE (NE, NE)	96.1 (93.7, 98.6)
12 months	NE (NE, NE)	96.1 (93.7, 98.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	1 (0.5)	11 (2.8)
Number of Subjects Censored, n (%)	196 (99.5)	386 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.068 (1.053)
95% CI		(0.517, 32.034)
Log-rank p-value		0.134

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.5, 100.0)	97.9 (96.4, 99.3)
6 months	99.5 (98.5, 100.0)	96.7 (94.4, 98.9)
9 months	NE (NE, NE)	95.8 (93.0, 98.6)
12 months	NE (NE, NE)	95.8 (93.0, 98.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	2 (1.0)	9 (2.3)
Number of Subjects Censored, n (%)	195 (99.0)	388 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.099 (0.782)
95% CI		(0.453, 9.730)
Log-rank p-value		0.364

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.5, 100.0)	97.6 (96.0, 99.1)
6 months	99.0 (97.5, 100.0)	97.6 (96.0, 99.1)
9 months	NE (NE, NE)	97.6 (96.0, 99.1)
12 months	NE (NE, NE)	97.6 (96.0, 99.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	1 (0.5)	9 (2.3)
Number of Subjects Censored, n (%)	196 (99.5)	388 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.446 (1.070)
95% CI		(0.300, 19.911)
Log-rank p-value		0.357

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	98.8 (97.6, 100.0)
6 months	99.4 (98.2, 100.0)	95.7 (92.7, 98.6)
9 months	NE (NE, NE)	95.7 (92.7, 98.6)
12 months	NE (NE, NE)	95.7 (92.7, 98.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	52 (26.4)	161 (40.6)
Number of Subjects Censored, n (%)	145 (73.6)	236 (59.4)
Time to first TEAE (months)		
25% percentile (95% CI)	2.73 (0.99, NE)	1.58 (0.95, 1.64)
Median (95% CI)	NE (5.82, NE)	7.85 (6.01, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.376 (0.161)
95% CI		(1.003, 1.888)
Log-rank p-value		0.045

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.5 (67.0, 79.9)	62.5 (57.6, 67.5)
6 months	56.8 (35.0, 78.5)	56.0 (50.2, 61.7)
9 months	NE (NE, NE)	49.1 (42.1, 56.2)
12 months	NE (NE, NE)	49.1 (42.1, 56.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.63	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	16 (8.1)	52 (13.1)
Number of Subjects Censored, n (%)	181 (91.9)	345 (86.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.82, NE)	NE (NE, NE)
Median (95% CI)	NE (5.82, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.303 (0.290)
95% CI		(0.737, 2.301)
Log-rank p-value		0.391

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.3 (85.5, 95.1)	88.4 (85.2, 91.7)
6 months	77.4 (53.6, 100.0)	84.3 (79.8, 88.7)
9 months	NE (NE, NE)	81.9 (76.6, 87.3)
12 months	NE (NE, NE)	81.9 (76.6, 87.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	9 (4.6)	43 (10.8)
Number of Subjects Censored, n (%)	188 (95.4)	354 (89.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.018 (0.371)
95% CI		(0.976, 4.171)
Log-rank p-value		0.052

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.3 (92.3, 98.3)	90.4 (87.3, 93.4)
6 months	95.3 (92.3, 98.3)	88.5 (85.0, 92.0)
9 months	NE (NE, NE)	85.3 (80.4, 90.2)
12 months	NE (NE, NE)	85.3 (80.4, 90.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	7 (3.6)	44 (11.1)
Number of Subjects Censored, n (%)	190 (96.4)	353 (88.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.495 (0.412)
95% CI		(1.113, 5.594)
Log-rank p-value		0.021

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.3 (93.7, 99.0)	90.9 (88.0, 93.9)
6 months	96.3 (93.7, 99.0)	87.8 (83.9, 91.6)
9 months	NE (NE, NE)	83.6 (78.2, 89.1)
12 months	NE (NE, NE)	83.6 (78.2, 89.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	10 (5.1)	33 (8.3)
Number of Subjects Censored, n (%)	187 (94.9)	364 (91.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.4, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.214 (0.367)
95% CI		(0.591, 2.494)
Log-rank p-value		0.691

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.8 (91.7, 97.9)	93.5 (91.0, 96.0)
6 months	94.8 (91.7, 97.9)	90.0 (86.5, 93.6)
9 months	NE (NE, NE)	87.7 (83.0, 92.4)
12 months	NE (NE, NE)	87.7 (83.0, 92.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	3 (1.5)	28 (7.1)
Number of Subjects Censored, n (%)	194 (98.5)	369 (92.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.488 (0.613)
95% CI		(1.048, 11.601)
Log-rank p-value		0.036

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (97.0, 100.0)	93.8 (91.3, 96.2)
6 months	95.9 (90.2, 100.0)	92.3 (89.1, 95.5)
9 months	NE (NE, NE)	88.4 (82.6, 94.1)
12 months	NE (NE, NE)	88.4 (82.6, 94.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	10 (5.1)	20 (5.0)
Number of Subjects Censored, n (%)	187 (94.9)	377 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.5, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.796 (0.394)
95% CI		(0.368, 1.722)
Log-rank p-value		0.509

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.2 (90.6, 97.8)	95.4 (93.3, 97.6)
6 months	94.2 (90.6, 97.8)	94.3 (91.7, 96.9)
9 months	NE (NE, NE)	93.4 (90.3, 96.6)
12 months	NE (NE, NE)	93.4 (90.3, 96.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	1 (0.5)	24 (6.0)
Number of Subjects Censored, n (%)	196 (99.5)	373 (94.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.5, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		10.227 (1.022)
95% CI		(1.379, 75.857)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.5, 100.0)	94.3 (91.9, 96.7)
6 months	99.5 (98.5, 100.0)	92.7 (89.7, 95.7)
9 months	NE (NE, NE)	92.7 (89.7, 95.7)
12 months	NE (NE, NE)	92.7 (89.7, 95.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	5 (2.5)	17 (4.3)
Number of Subjects Censored, n (%)	192 (97.5)	380 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.308 (0.515)
95% CI		(0.476, 3.591)
Log-rank p-value		0.590

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (95.1, 100.0)	95.9 (93.8, 97.9)
6 months	94.8 (89.0, 100.0)	95.1 (92.6, 97.6)
9 months	NE (NE, NE)	94.3 (91.3, 97.3)
12 months	NE (NE, NE)	94.3 (91.3, 97.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	1 (0.5)	12 (3.0)
Number of Subjects Censored, n (%)	196 (99.5)	385 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.736 (1.044)
95% CI		(0.611, 36.682)
Log-rank p-value		0.103

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.4, 100.0)	96.9 (95.0, 98.7)
6 months	99.5 (98.4, 100.0)	96.3 (94.2, 98.4)
9 months	NE (NE, NE)	96.3 (94.2, 98.4)
12 months	NE (NE, NE)	96.3 (94.2, 98.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	2 (1.0)	10 (2.5)
Number of Subjects Censored, n (%)	195 (99.0)	387 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.149 (0.775)
95% CI		(0.470, 9.820)
Log-rank p-value		0.306

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.5, 100.0)	97.3 (95.6, 98.9)
6 months	99.0 (97.5, 100.0)	97.3 (95.6, 98.9)
9 months	NE (NE, NE)	97.3 (95.6, 98.9)
12 months	NE (NE, NE)	97.3 (95.6, 98.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	44 (22.3)	156 (39.3)
Number of Subjects Censored, n (%)	153 (77.7)	241 (60.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.54, NE)	0.72 (0.69, 1.45)
Median (95% CI)	NE (NE, NE)	11.53 (6.41, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.718 (0.172)
95% CI		(1.226, 2.407)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.2 (70.0, 82.5)	64.0 (59.2, 68.8)
6 months	76.2 (70.0, 82.5)	58.2 (52.6, 63.7)
9 months	NE (NE, NE)	55.7 (49.8, 61.7)
12 months	NE (NE, NE)	49.0 (38.3, 59.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.40	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	10 (5.1)	66 (16.6)
Number of Subjects Censored, n (%)	187 (94.9)	331 (83.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.407 (0.340)
95% CI		(1.751, 6.629)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (91.0, 97.8)	83.3 (79.6, 87.1)
6 months	94.4 (91.0, 97.8)	82.9 (79.1, 86.7)
9 months	NE (NE, NE)	82.9 (79.1, 86.7)
12 months	NE (NE, NE)	82.9 (79.1, 86.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	18 (9.1)	38 (9.6)
Number of Subjects Censored, n (%)	179 (90.9)	359 (90.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	14.32 (14.32, NE)
Median (95% CI)	NE (NE, NE)	NE (14.32, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (14.32, NE)
Min, Max	0.0, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.812 (0.292)
95% CI		(0.458, 1.441)
Log-rank p-value		0.434

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.4 (86.1, 94.6)	92.3 (89.6, 95.0)
6 months	90.4 (86.1, 94.6)	89.1 (85.4, 92.8)
9 months	NE (NE, NE)	87.4 (83.2, 91.7)
12 months	NE (NE, NE)	87.4 (83.2, 91.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	16 (8.1)	34 (8.6)
Number of Subjects Censored, n (%)	181 (91.9)	363 (91.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.888 (0.308)
95% CI		(0.486, 1.624)
Log-rank p-value		0.674

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.2 (87.1, 95.4)	92.1 (89.4, 94.9)
6 months	91.2 (87.1, 95.4)	91.1 (88.1, 94.2)
9 months	NE (NE, NE)	90.2 (86.8, 93.7)
12 months	NE (NE, NE)	84.2 (72.4, 96.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	2 (1.0)	16 (4.0)
Number of Subjects Censored, n (%)	195 (99.0)	381 (96.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.573 (0.750)
95% CI		(0.821, 15.550)
Log-rank p-value		0.077

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.6, 100.0)	95.7 (93.7, 97.8)
6 months	99.0 (97.6, 100.0)	95.7 (93.7, 97.8)
9 months	NE (NE, NE)	95.7 (93.7, 97.8)
12 months	NE (NE, NE)	95.7 (93.7, 97.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	1 (0.5)	10 (2.5)
Number of Subjects Censored, n (%)	196 (99.5)	387 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.2, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.619 (1.063)
95% CI		(0.450, 29.095)
Log-rank p-value		0.212

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.5, 100.0)	98.2 (96.9, 99.5)
6 months	99.5 (98.5, 100.0)	97.6 (95.7, 99.4)
9 months	NE (NE, NE)	95.4 (92.0, 98.9)
12 months	NE (NE, NE)	95.4 (92.0, 98.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Vascular disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	29 (14.7)	158 (39.8)
Number of Subjects Censored, n (%)	168 (85.3)	239 (60.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.61, NE)	0.95 (0.69, 1.45)
Median (95% CI)	NE (NE, NE)	NE (6.93, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.819 (0.203)
95% CI		(1.894, 4.195)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Vascular disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.4 (79.0, 89.8)	61.1 (56.1, 66.0)
6 months	81.5 (73.8, 89.1)	57.8 (52.3, 63.3)
9 months	NE (NE, NE)	52.6 (45.6, 59.6)
12 months	NE (NE, NE)	52.6 (45.6, 59.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	2.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	15 (7.6)	147 (37.0)
Number of Subjects Censored, n (%)	182 (92.4)	250 (63.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.99 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	NE (7.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.177 (0.272)
95% CI		(3.040, 8.818)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.4 (87.2, 95.6)	63.7 (58.8, 68.6)
6 months	91.4 (87.2, 95.6)	61.8 (56.7, 67.0)
9 months	NE (NE, NE)	55.3 (48.1, 62.5)
12 months	NE (NE, NE)	55.3 (48.1, 62.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	2.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	42 (21.3)	140 (35.3)
Number of Subjects Censored, n (%)	155 (78.7)	257 (64.7)
Time to first TEAE (months)		
25% percentile (95% CI)	3.71 (1.87, NE)	1.61 (0.95, 2.00)
Median (95% CI)	NE (NE, NE)	NE (8.64, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.570 (0.179)
95% CI		(1.105, 2.231)
Log-rank p-value		0.011

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.7 (71.4, 83.9)	66.4 (61.7, 71.2)
6 months	71.9 (62.3, 81.5)	61.8 (56.2, 67.4)
9 months	NE (NE, NE)	55.1 (46.7, 63.5)
12 months	NE (NE, NE)	51.2 (40.4, 61.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.46	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	16 (8.1)	45 (11.3)
Number of Subjects Censored, n (%)	181 (91.9)	352 (88.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.240 (0.301)
95% CI		(0.687, 2.237)
Log-rank p-value		0.486

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.5 (87.5, 95.5)	89.4 (86.3, 92.6)
6 months	91.5 (87.5, 95.5)	86.9 (83.1, 90.7)
9 months	NE (NE, NE)	86.0 (81.9, 90.2)
12 months	NE (NE, NE)	86.0 (81.9, 90.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	7 (3.6)	46 (11.6)
Number of Subjects Censored, n (%)	190 (96.4)	351 (88.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.721 (0.409)
95% CI		(1.221, 6.067)
Log-rank p-value		0.011

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.2 (93.4, 99.0)	90.0 (87.0, 93.0)
6 months	96.2 (93.4, 99.0)	86.9 (82.9, 91.0)
9 months	NE (NE, NE)	82.7 (76.6, 88.8)
12 months	NE (NE, NE)	82.7 (76.6, 88.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	4 (2.0)	23 (5.8)
Number of Subjects Censored, n (%)	193 (98.0)	374 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.419 (0.545)
95% CI		(0.832, 7.037)
Log-rank p-value		0.085

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.6, 100.0)	94.5 (92.2, 96.8)
6 months	93.5 (85.9, 100.0)	93.0 (90.0, 96.1)
9 months	NE (NE, NE)	93.0 (90.0, 96.1)
12 months	NE (NE, NE)	93.0 (90.0, 96.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	4 (2.0)	13 (3.3)
Number of Subjects Censored, n (%)	193 (98.0)	384 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.402 (0.577)
95% CI		(0.452, 4.346)
Log-rank p-value		0.597

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.9 (95.8, 99.9)	96.8 (95.0, 98.6)
6 months	97.9 (95.8, 99.9)	96.0 (93.5, 98.4)
9 months	NE (NE, NE)	96.0 (93.5, 98.4)
12 months	NE (NE, NE)	96.0 (93.5, 98.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	2 (1.0)	10 (2.5)
Number of Subjects Censored, n (%)	195 (99.0)	387 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.774 (0.797)
95% CI		(0.372, 8.465)
Log-rank p-value		0.459

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.5, 100.0)	98.2 (96.8, 99.5)
6 months	99.0 (97.5, 100.0)	97.4 (95.4, 99.4)
9 months	NE (NE, NE)	93.6 (87.8, 99.3)
12 months	NE (NE, NE)	93.6 (87.8, 99.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	0	9 (2.3)
Number of Subjects Censored, n (%)	197 (100.0)	388 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.057

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.5 (95.9, 99.1)
6 months	100.0 (100.0, 100.0)	97.5 (95.9, 99.1)
9 months	NE (NE, NE)	97.5 (95.9, 99.1)
12 months	NE (NE, NE)	97.5 (95.9, 99.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	23 (11.7)	142 (35.8)
Number of Subjects Censored, n (%)	174 (88.3)	255 (64.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.45 (0.95, 1.64)
Median (95% CI)	NE (NE, NE)	13.14 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	13.14 (NE, NE)
Min, Max	0.1, 8.4*	0.0, 13.1
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.306 (0.230)
95% CI		(2.107, 5.188)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.4 (83.9, 93.0)	65.9 (61.1, 70.7)
6 months	85.5 (78.3, 92.7)	60.1 (54.5, 65.7)
9 months	NE (NE, NE)	60.1 (54.5, 65.7)
12 months	NE (NE, NE)	60.1 (54.5, 65.7)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.69	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	3 (1.5)	79 (19.9)
Number of Subjects Censored, n (%)	194 (98.5)	318 (80.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.84, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		19.234 (0.716)
95% CI		(4.723, 78.325)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.7, 100.0)	81.9 (78.0, 85.7)
6 months	98.5 (96.7, 100.0)	76.6 (71.6, 81.6)
9 months	NE (NE, NE)	76.6 (71.6, 81.6)
12 months	NE (NE, NE)	76.6 (71.6, 81.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	6 (3.0)	17 (4.3)
Number of Subjects Censored, n (%)	191 (97.0)	380 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.309 (0.476)
95% CI		(0.515, 3.330)
Log-rank p-value		0.584

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (94.5, 99.3)	95.5 (93.4, 97.6)
6 months	96.9 (94.5, 99.3)	95.5 (93.4, 97.6)
9 months	NE (NE, NE)	95.5 (93.4, 97.6)
12 months	NE (NE, NE)	95.5 (93.4, 97.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	3 (1.5)	12 (3.0)
Number of Subjects Censored, n (%)	194 (98.5)	385 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.741 (0.651)
95% CI		(0.486, 6.229)
Log-rank p-value		0.435

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (97.3, 100.0)	97.1 (95.4, 98.8)
6 months	96.1 (90.4, 100.0)	96.6 (94.7, 98.5)
9 months	NE (NE, NE)	96.6 (94.7, 98.5)
12 months	NE (NE, NE)	96.6 (94.7, 98.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Nervous system disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	35 (17.8)	102 (25.7)
Number of Subjects Censored, n (%)	162 (82.2)	295 (74.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.50, NE)	4.14 (2.07, 6.11)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.269 (0.198)
95% CI		(0.861, 1.871)
Log-rank p-value		0.279

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Nervous system disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.6 (74.7, 86.5)	77.0 (72.8, 81.3)
6 months	80.6 (74.7, 86.5)	70.5 (65.1, 75.9)
9 months	NE (NE, NE)	68.8 (63.0, 74.6)
12 months	NE (NE, NE)	64.7 (55.3, 74.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.50	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	10 (5.1)	37 (9.3)
Number of Subjects Censored, n (%)	187 (94.9)	360 (90.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.671 (0.359)
95% CI		(0.827, 3.377)
Log-rank p-value		0.156

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.2 (90.7, 97.8)	91.5 (88.8, 94.3)
6 months	94.2 (90.7, 97.8)	90.4 (87.2, 93.6)
9 months	NE (NE, NE)	88.6 (84.7, 92.6)
12 months	NE (NE, NE)	88.6 (84.7, 92.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	7 (3.6)	9 (2.3)
Number of Subjects Censored, n (%)	190 (96.4)	388 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.594 (0.505)
95% CI		(0.221, 1.597)
Log-rank p-value		0.292

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.4 (93.7, 99.0)	97.6 (96.1, 99.2)
6 months	96.4 (93.7, 99.0)	97.6 (96.1, 99.2)
9 months	NE (NE, NE)	97.6 (96.1, 99.2)
12 months	NE (NE, NE)	97.6 (96.1, 99.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	4 (2.0)	10 (2.5)
Number of Subjects Censored, n (%)	193 (98.0)	387 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.2, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.224 (0.592)
95% CI		(0.384, 3.904)
Log-rank p-value		0.766

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.6, 99.9)	97.5 (95.9, 99.0)
6 months	97.8 (95.6, 99.9)	97.5 (95.9, 99.0)
9 months	NE (NE, NE)	97.5 (95.9, 99.0)
12 months	NE (NE, NE)	97.5 (95.9, 99.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	24 (12.2)	100 (25.2)
Number of Subjects Censored, n (%)	173 (87.8)	297 (74.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	3.91 (2.76, 6.93)
Median (95% CI)	NE (NE, NE)	13.60 (11.96, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.0, 8.4*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.718 (0.230)
95% CI		(1.095, 2.697)
Log-rank p-value		0.021

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.9 (81.8, 92.0)	78.1 (73.9, 82.3)
6 months	83.8 (76.1, 91.6)	71.0 (65.6, 76.4)
9 months	NE (NE, NE)	68.7 (62.6, 74.8)
12 months	NE (NE, NE)	60.1 (43.5, 76.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	8 (4.1)	70 (17.6)
Number of Subjects Censored, n (%)	189 (95.9)	327 (82.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.60 (5.78, NE)
Median (95% CI)	NE (NE, NE)	13.60 (13.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.2*, 8.4*	0.2, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.647 (0.375)
95% CI		(1.747, 7.611)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (92.8, 98.6)	84.5 (80.8, 88.2)
6 months	95.7 (92.8, 98.6)	79.6 (74.9, 84.4)
9 months	NE (NE, NE)	76.3 (69.7, 82.8)
12 months	NE (NE, NE)	76.3 (69.7, 82.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	5 (2.5)	9 (2.3)
Number of Subjects Censored, n (%)	192 (97.5)	388 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.4, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.735 (0.562)
95% CI		(0.244, 2.213)
Log-rank p-value		0.545

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (95.0, 99.6)	97.9 (96.5, 99.3)
6 months	97.3 (95.0, 99.6)	97.4 (95.7, 99.1)
9 months	NE (NE, NE)	97.4 (95.7, 99.1)
12 months	NE (NE, NE)	97.4 (95.7, 99.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Infections and infestations**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	26 (13.2)	83 (20.9)
Number of Subjects Censored, n (%)	171 (86.8)	314 (79.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	5.91 (4.63, 6.93)
Median (95% CI)	NE (NE, NE)	NE (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.141 (0.235)
95% CI		(0.720, 1.807)
Log-rank p-value		0.526

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Infections and infestations**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.3 (82.4, 92.2)	84.2 (80.4, 88.0)
6 months	77.9 (66.5, 89.3)	74.3 (68.5, 80.2)
9 months	NE (NE, NE)	64.2 (55.8, 72.7)
12 months	NE (NE, NE)	58.4 (45.0, 71.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	8 (4.1)	16 (4.0)
Number of Subjects Censored, n (%)	189 (95.9)	381 (96.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.14, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.2, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.638 (0.454)
95% CI		(0.262, 1.554)
Log-rank p-value		0.459

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.9 (96.0, 99.9)	96.8 (95.1, 98.6)
6 months	85.4 (73.3, 97.5)	96.0 (93.6, 98.4)
9 months	NE (NE, NE)	92.9 (88.8, 97.1)
12 months	NE (NE, NE)	92.9 (88.8, 97.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	5 (2.5)	12 (3.0)
Number of Subjects Censored, n (%)	192 (97.5)	385 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.56, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.608 (0.560)
95% CI		(0.203, 1.822)
Log-rank p-value		0.323

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (95.3, 100.0)	98.6 (97.3, 99.8)
6 months	93.7 (85.9, 100.0)	95.8 (93.1, 98.5)
9 months	NE (NE, NE)	94.8 (91.5, 98.1)
12 months	NE (NE, NE)	88.9 (77.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	1 (0.5)	8 (2.0)
Number of Subjects Censored, n (%)	196 (99.5)	389 (98.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.831 (1.067)
95% CI		(0.350, 22.898)
Log-rank p-value		0.336

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.5, 100.0)	97.9 (96.3, 99.5)
6 months	99.5 (98.5, 100.0)	97.1 (94.9, 99.3)
9 months	NE (NE, NE)	97.1 (94.9, 99.3)
12 months	NE (NE, NE)	97.1 (94.9, 99.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	32 (16.2)	59 (14.9)
Number of Subjects Censored, n (%)	165 (83.8)	338 (85.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.77, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.726 (0.224)
95% CI		(0.468, 1.125)
Log-rank p-value		0.178

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.9 (76.1, 87.7)	86.9 (83.4, 90.3)
6 months	81.9 (76.1, 87.7)	82.6 (77.9, 87.2)
9 months	NE (NE, NE)	79.6 (74.1, 85.1)
12 months	NE (NE, NE)	79.6 (74.1, 85.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.63	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	23 (11.7)	32 (8.1)
Number of Subjects Censored, n (%)	174 (88.3)	365 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.490 (0.282)
95% CI		(0.282, 0.851)
Log-rank p-value		0.014

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.5 (81.2, 91.8)	93.7 (91.2, 96.2)
6 months	86.5 (81.2, 91.8)	89.3 (85.3, 93.4)
9 months	NE (NE, NE)	87.6 (83.0, 92.2)
12 months	NE (NE, NE)	87.6 (83.0, 92.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	3 (1.5)	24 (6.0)
Number of Subjects Censored, n (%)	194 (98.5)	373 (94.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.808 (0.613)
95% CI		(1.145, 12.662)
Log-rank p-value		0.019

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.5, 100.0)	93.6 (91.2, 96.1)
6 months	98.4 (96.5, 100.0)	93.6 (91.2, 96.1)
9 months	NE (NE, NE)	93.6 (91.2, 96.1)
12 months	NE (NE, NE)	93.6 (91.2, 96.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Endocrine disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	1 (0.5)	86 (21.7)
Number of Subjects Censored, n (%)	196 (99.5)	311 (78.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.68 (3.81, 6.90)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		35.814 (1.007)
95% CI		(4.981, 257.524)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Endocrine disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.5, 100.0)	81.6 (77.6, 85.6)
6 months	99.5 (98.5, 100.0)	71.4 (65.3, 77.6)
9 months	NE (NE, NE)	68.2 (61.3, 75.1)
12 months	NE (NE, NE)	68.2 (61.3, 75.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	1 (0.5)	81 (20.4)
Number of Subjects Censored, n (%)	196 (99.5)	316 (79.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.75 (4.17, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		33.307 (1.007)
95% CI		(4.628, 239.720)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.5, 100.0)	82.9 (79.1, 86.8)
6 months	99.5 (98.5, 100.0)	72.8 (66.8, 78.9)
9 months	NE (NE, NE)	69.6 (62.8, 76.4)
12 months	NE (NE, NE)	69.6 (62.8, 76.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Psychiatric disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	14 (7.1)	48 (12.1)
Number of Subjects Censored, n (%)	183 (92.9)	349 (87.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.283 (0.307)
95% CI		(0.702, 2.343)
Log-rank p-value		0.416

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Psychiatric disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.6 (88.8, 96.5)	89.7 (86.5, 92.9)
6 months	90.7 (85.4, 96.1)	84.1 (79.6, 88.7)
9 months	NE (NE, NE)	83.1 (78.1, 88.0)
12 months	NE (NE, NE)	83.1 (78.1, 88.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	9 (4.6)	22 (5.5)
Number of Subjects Censored, n (%)	188 (95.4)	375 (94.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.848 (0.401)
95% CI		(0.387, 1.861)
Log-rank p-value		0.678

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (91.6, 98.2)	95.3 (93.0, 97.6)
6 months	94.9 (91.6, 98.2)	92.8 (89.6, 95.9)
9 months	NE (NE, NE)	91.7 (87.9, 95.4)
12 months	NE (NE, NE)	91.7 (87.9, 95.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	2 (1.0)	10 (2.5)
Number of Subjects Censored, n (%)	195 (99.0)	387 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.839 (0.780)
95% CI		(0.399, 8.480)
Log-rank p-value		0.445

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	97.3 (95.6, 99.1)
6 months	97.4 (93.3, 100.0)	96.7 (94.5, 98.8)
9 months	NE (NE, NE)	96.7 (94.5, 98.8)
12 months	NE (NE, NE)	96.7 (94.5, 98.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	2 (1.0)	7 (1.8)
Number of Subjects Censored, n (%)	195 (99.0)	390 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.3, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.494 (0.808)
95% CI		(0.306, 7.285)
Log-rank p-value		0.624

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (97.0, 100.0)	98.4 (97.1, 99.7)
6 months	98.8 (97.0, 100.0)	97.7 (95.7, 99.6)
9 months	NE (NE, NE)	97.7 (95.7, 99.6)
12 months	NE (NE, NE)	97.7 (95.7, 99.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	22 (11.2)	44 (11.1)
Number of Subjects Censored, n (%)	175 (88.8)	353 (88.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.66, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.763 (0.265)
95% CI		(0.454, 1.283)
Log-rank p-value		0.284

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.8 (84.3, 93.3)	89.5 (86.3, 92.7)
6 months	86.9 (81.2, 92.7)	86.6 (82.6, 90.6)
9 months	NE (NE, NE)	86.6 (82.6, 90.6)
12 months	NE (NE, NE)	83.4 (76.1, 90.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	3 (1.5)	19 (4.8)
Number of Subjects Censored, n (%)	194 (98.5)	378 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.264 (0.628)
95% CI		(0.662, 7.745)
Log-rank p-value		0.193

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (96.3, 100.0)	95.4 (93.2, 97.6)
6 months	98.3 (96.3, 100.0)	94.1 (91.3, 96.9)
9 months	NE (NE, NE)	94.1 (91.3, 96.9)
12 months	NE (NE, NE)	90.7 (83.4, 97.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Number of Subjects with Events, n (%)	2 (1.0)	11 (2.8)
Number of Subjects Censored, n (%)	195 (99.0)	386 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.244 (0.772)
95% CI		(0.494, 10.186)
Log-rank p-value		0.290

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
WT (Wild Type)

Statistics	Placebo + BSC N=197	Fruquintinib + BSC N=397
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.5, 100.0)	97.3 (95.7, 99.0)
6 months	99.0 (97.5, 100.0)	96.8 (94.9, 98.7)
9 months	NE (NE, NE)	96.8 (94.9, 98.7)
12 months	NE (NE, NE)	96.8 (94.9, 98.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	6 (60.0)	1 (14.3)
Number of Subjects Censored, n (%)	4 (40.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	0.46 (0.03, 1.48)	NE (0.69, NE)
Median (95% CI)	1.22 (0.03, NE)	NE (0.69, NE)
75% percentile (95% CI)	NE (0.95, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.7, 7.0*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.097 (1.289)
95% CI		(0.008, 1.213)
Log-rank p-value		0.191

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	40.0 (9.6, 70.4)	85.7 (59.8, 100.0)
6 months	40.0 (9.6, 70.4)	85.7 (59.8, 100.0)
9 months	40.0 (9.6, 70.4)	NE (NE, NE)
12 months	40.0 (9.6, 70.4)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.22	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	4 (40.0)	1 (14.3)
Number of Subjects Censored, n (%)	6 (60.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	0.46 (0.03, NE)	NE (0.69, NE)
Median (95% CI)	NE (0.03, NE)	NE (0.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.7, 7.0*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.183 (1.266)
95% CI		(0.015, 2.193)
Log-rank p-value		0.359

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	60.0 (29.6, 90.4)	85.7 (59.8, 100.0)
6 months	60.0 (29.6, 90.4)	85.7 (59.8, 100.0)
9 months	60.0 (29.6, 90.4)	NE (NE, NE)
12 months	60.0 (29.6, 90.4)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.48	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	2 (20.0)	0
Number of Subjects Censored, n (%)	8 (80.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (NE, NE)
Median (95% CI)	NE (0.95, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.8 (50.6, 100.0)	100.0 (100.0, 100.0)
6 months	77.8 (50.6, 100.0)	100.0 (100.0, 100.0)
9 months	77.8 (50.6, 100.0)	NE (NE, NE)
12 months	77.8 (50.6, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	1 (10.0)	0
Number of Subjects Censored, n (%)	9 (90.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.71, NE)	NE (NE, NE)
Median (95% CI)	NE (1.71, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (68.4, 100.0)	100.0 (100.0, 100.0)
6 months	88.9 (68.4, 100.0)	100.0 (100.0, 100.0)
9 months	88.9 (68.4, 100.0)	NE (NE, NE)
12 months	88.9 (68.4, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.71	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	1 (10.0)	0
Number of Subjects Censored, n (%)	9 (90.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.82, NE)	NE (NE, NE)
Median (95% CI)	NE (0.82, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8, 13.0*	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (71.4, 100.0)	100.0 (100.0, 100.0)
6 months	90.0 (71.4, 100.0)	100.0 (100.0, 100.0)
9 months	90.0 (71.4, 100.0)	NE (NE, NE)
12 months	90.0 (71.4, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	1 (10.0)	0
Number of Subjects Censored, n (%)	9 (90.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.49, NE)	NE (NE, NE)
Median (95% CI)	NE (0.49, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 13.0*	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (71.4, 100.0)	100.0 (100.0, 100.0)
6 months	90.0 (71.4, 100.0)	100.0 (100.0, 100.0)
9 months	90.0 (71.4, 100.0)	NE (NE, NE)
12 months	90.0 (71.4, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	4 (40.0)	5 (71.4)
Number of Subjects Censored, n (%)	6 (60.0)	2 (28.6)
Time to first TEAE (months)		
25% percentile (95% CI)	2.00 (0.46, NE)	0.69 (0.03, 1.87)
Median (95% CI)	5.59 (0.46, NE)	1.87 (0.03, NE)
75% percentile (95% CI)	5.59 (NE, NE)	5.03 (1.84, NE)
Min, Max	0.5, 5.6	0.0, 5.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.373 (1.035)
95% CI		(0.706, 40.867)
Log-rank p-value		0.239

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	68.6 (38.9, 98.3)	42.9 (6.2, 79.5)
6 months	0.0 (NE, NE)	NE (NE, NE)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.71	1.87

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	0	2 (28.6)
Number of Subjects Censored, n (%)	10 (100.0)	5 (71.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.84 (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (0.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	0.7, 7.0*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.090

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	71.4 (38.0, 100.0)
6 months	100.0 (100.0, 100.0)	71.4 (38.0, 100.0)
9 months	100.0 (100.0, 100.0)	NE (NE, NE)
12 months	100.0 (100.0, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	1 (10.0)	2 (28.6)
Number of Subjects Censored, n (%)	9 (90.0)	5 (71.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.46, NE)	5.73 (5.03, NE)
Median (95% CI)	NE (0.46, NE)	6.44 (5.03, NE)
75% percentile (95% CI)	NE (NE, NE)	6.44 (5.03, NE)
Min, Max	0.5, 13.0*	1.9*, 6.4
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.618 (1.530)
95% CI		(0.081, 32.474)
Log-rank p-value		1.000

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (71.4, 100.0)	100.0 (100.0, 100.0)
6 months	90.0 (71.4, 100.0)	75.0 (32.6, 100.0)
9 months	90.0 (71.4, 100.0)	0.0 (NE, NE)
12 months	90.0 (71.4, 100.0)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.71	5.03

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	0	2 (28.6)
Number of Subjects Censored, n (%)	10 (100.0)	5 (71.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.69 (0.03, NE)
Median (95% CI)	NE (NE, NE)	NE (0.03, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	0.0, 7.0*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.018

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	71.4 (38.0, 100.0)
6 months	100.0 (100.0, 100.0)	71.4 (38.0, 100.0)
9 months	100.0 (100.0, 100.0)	NE (NE, NE)
12 months	100.0 (100.0, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	0	1 (14.3)
Number of Subjects Censored, n (%)	10 (100.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.03, NE)
Median (95% CI)	NE (NE, NE)	NE (0.03, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	0.0, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.157

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	85.7 (59.8, 100.0)
6 months	100.0 (100.0, 100.0)	85.7 (59.8, 100.0)
9 months	100.0 (100.0, 100.0)	NE (NE, NE)
12 months	100.0 (100.0, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	1 (10.0)	2 (28.6)
Number of Subjects Censored, n (%)	9 (90.0)	5 (71.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.97, NE)	1.81 (0.03, NE)
Median (95% CI)	NE (1.97, NE)	NE (0.03, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	0.0, 7.0*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		7.654 (1.452)
95% CI		(0.445, 131.800)
Log-rank p-value		0.224

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (68.4, 100.0)	71.4 (38.0, 100.0)
6 months	88.9 (68.4, 100.0)	71.4 (38.0, 100.0)
9 months	88.9 (68.4, 100.0)	NE (NE, NE)
12 months	88.9 (68.4, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.71	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	0	1 (14.3)
Number of Subjects Censored, n (%)	10 (100.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.87, NE)
Median (95% CI)	NE (NE, NE)	NE (1.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	1.9, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	85.7 (59.8, 100.0)
6 months	100.0 (100.0, 100.0)	85.7 (59.8, 100.0)
9 months	100.0 (100.0, 100.0)	NE (NE, NE)
12 months	100.0 (100.0, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	1 (10.0)	0
Number of Subjects Censored, n (%)	9 (90.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (NE, NE)	NE (NE, NE)
Median (95% CI)	5.59 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	5.59 (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 5.6	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	0.0 (NE, NE)	100.0 (100.0, 100.0)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	0	1 (14.3)
Number of Subjects Censored, n (%)	10 (100.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.87, NE)
Median (95% CI)	NE (NE, NE)	NE (1.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	1.9, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	85.7 (59.8, 100.0)
6 months	100.0 (100.0, 100.0)	85.7 (59.8, 100.0)
9 months	100.0 (100.0, 100.0)	NE (NE, NE)
12 months	100.0 (100.0, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	4 (40.0)	1 (14.3)
Number of Subjects Censored, n (%)	6 (60.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.66, NE)	NE (0.69, NE)
Median (95% CI)	10.18 (0.66, NE)	NE (0.69, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.7, 10.2	0.7, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.656 (1.183)
95% CI		(0.065, 6.673)
Log-rank p-value		0.841

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	67.5 (37.1, 97.9)	85.7 (59.8, 100.0)
6 months	67.5 (37.1, 97.9)	85.7 (59.8, 100.0)
9 months	67.5 (37.1, 97.9)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.40	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	2 (20.0)	0
Number of Subjects Censored, n (%)	8 (80.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.66, NE)	NE (NE, NE)
Median (95% CI)	NE (0.66, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 13.0*	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.225

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.8 (52.5, 100.0)	100.0 (100.0, 100.0)
6 months	78.8 (52.5, 100.0)	100.0 (100.0, 100.0)
9 months	78.8 (52.5, 100.0)	NE (NE, NE)
12 months	78.8 (52.5, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.71	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	2 (20.0)	0
Number of Subjects Censored, n (%)	8 (80.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (NE, NE)
Median (95% CI)	NE (0.95, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.8 (50.6, 100.0)	100.0 (100.0, 100.0)
6 months	77.8 (50.6, 100.0)	100.0 (100.0, 100.0)
9 months	77.8 (50.6, 100.0)	NE (NE, NE)
12 months	77.8 (50.6, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	0	1 (14.3)
Number of Subjects Censored, n (%)	10 (100.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (0.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	0.7, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	85.7 (59.8, 100.0)
6 months	100.0 (100.0, 100.0)	85.7 (59.8, 100.0)
9 months	100.0 (100.0, 100.0)	NE (NE, NE)
12 months	100.0 (100.0, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	1 (10.0)	0
Number of Subjects Censored, n (%)	9 (90.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Median (95% CI)	10.18 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 10.2	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
9 months	100.0 (100.0, 100.0)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	0	1 (14.3)
Number of Subjects Censored, n (%)	10 (100.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (0.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	0.7, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	85.7 (59.8, 100.0)
6 months	100.0 (100.0, 100.0)	85.7 (59.8, 100.0)
9 months	100.0 (100.0, 100.0)	NE (NE, NE)
12 months	100.0 (100.0, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	5 (50.0)	4 (57.1)
Number of Subjects Censored, n (%)	5 (50.0)	3 (42.9)
Time to first TEAE (months)		
25% percentile (95% CI)	1.71 (0.69, NE)	2.23 (0.69, NE)
Median (95% CI)	5.59 (0.69, NE)	6.90 (0.69, NE)
75% percentile (95% CI)	5.59 (2.17, NE)	6.90 (2.23, NE)
Min, Max	0.7, 5.6	0.7, 6.9
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.562 (0.895)
95% CI		(0.097, 3.243)
Log-rank p-value		0.636

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	56.3 (23.9, 88.6)	51.4 (11.5, 91.4)
6 months	0.0 (NE, NE)	51.4 (11.5, 91.4)
9 months	0.0 (NE, NE)	0.0 (NE, NE)
12 months	0.0 (NE, NE)	0.0 (NE, NE)
18 months	0.0 (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.18	2.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	4 (40.0)	0
Number of Subjects Censored, n (%)	6 (60.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	2.17 (0.69, NE)	NE (NE, NE)
Median (95% CI)	5.59 (0.69, NE)	NE (NE, NE)
75% percentile (95% CI)	5.59 (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.105

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	67.5 (37.1, 97.9)	100.0 (100.0, 100.0)
6 months	0.0 (NE, NE)	100.0 (100.0, 100.0)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.40	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	1 (10.0)	0
Number of Subjects Censored, n (%)	9 (90.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (NE, NE)	NE (NE, NE)
Median (95% CI)	5.59 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	5.59 (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 5.6	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	0.0 (NE, NE)	100.0 (100.0, 100.0)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	1 (10.0)	0
Number of Subjects Censored, n (%)	9 (90.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (NE, NE)	NE (NE, NE)
Median (95% CI)	5.59 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	5.59 (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 5.6	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	0.0 (NE, NE)	100.0 (100.0, 100.0)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	0	1 (14.3)
Number of Subjects Censored, n (%)	10 (100.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (0.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	0.7, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	85.7 (59.8, 100.0)
6 months	100.0 (100.0, 100.0)	85.7 (59.8, 100.0)
9 months	100.0 (100.0, 100.0)	NE (NE, NE)
12 months	100.0 (100.0, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	0	1 (14.3)
Number of Subjects Censored, n (%)	10 (100.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.23, NE)
Median (95% CI)	NE (NE, NE)	NE (2.23, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	83.3 (53.5, 100.0)
6 months	100.0 (100.0, 100.0)	83.3 (53.5, 100.0)
9 months	100.0 (100.0, 100.0)	NE (NE, NE)
12 months	100.0 (100.0, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	1 (10.0)	0
Number of Subjects Censored, n (%)	9 (90.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	7.43 (NE, NE)	NE (NE, NE)
Median (95% CI)	7.43 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	7.43 (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 7.4	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	0	1 (14.3)
Number of Subjects Censored, n (%)	10 (100.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.71, NE)
Median (95% CI)	NE (NE, NE)	NE (3.71, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	100.0 (100.0, 100.0)	83.3 (53.5, 100.0)
9 months	100.0 (100.0, 100.0)	NE (NE, NE)
12 months	100.0 (100.0, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	0	1 (14.3)
Number of Subjects Censored, n (%)	10 (100.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	6.90 (6.90, NE)
Median (95% CI)	NE (NE, NE)	NE (6.90, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (6.90, NE)
Min, Max	0.8*, 13.0*	1.9*, 7.0*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
9 months	100.0 (100.0, 100.0)	NE (NE, NE)
12 months	100.0 (100.0, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	0	1 (14.3)
Number of Subjects Censored, n (%)	10 (100.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	6.90 (6.90, NE)
Median (95% CI)	NE (NE, NE)	NE (6.90, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (6.90, NE)
Min, Max	0.8*, 13.0*	1.9*, 7.0*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
9 months	100.0 (100.0, 100.0)	NE (NE, NE)
12 months	100.0 (100.0, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	4 (40.0)	2 (28.6)
Number of Subjects Censored, n (%)	6 (60.0)	5 (71.4)
Time to first TEAE (months)		
25% percentile (95% CI)	1.48 (0.03, NE)	1.64 (0.69, NE)
Median (95% CI)	NE (0.03, NE)	NE (0.69, NE)
75% percentile (95% CI)	NE (1.84, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.7, 7.0*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.415 (1.121)
95% CI		(0.046, 3.731)
Log-rank p-value		0.403

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	57.1 (25.0, 89.2)	71.4 (38.0, 100.0)
6 months	57.1 (25.0, 89.2)	71.4 (38.0, 100.0)
9 months	57.1 (25.0, 89.2)	NE (NE, NE)
12 months	57.1 (25.0, 89.2)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.02	4.57

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	0	1 (14.3)
Number of Subjects Censored, n (%)	10 (100.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.95, NE)
Median (95% CI)	NE (NE, NE)	NE (0.95, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	1.0, 7.0*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.157

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	85.7 (59.8, 100.0)
6 months	100.0 (100.0, 100.0)	85.7 (59.8, 100.0)
9 months	100.0 (100.0, 100.0)	NE (NE, NE)
12 months	100.0 (100.0, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	2 (20.0)	1 (14.3)
Number of Subjects Censored, n (%)	8 (80.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	NE (1.64, NE)
Median (95% CI)	NE (0.03, NE)	NE (1.64, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	1.6, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.000 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.281

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.0 (55.2, 100.0)	85.7 (59.8, 100.0)
6 months	80.0 (55.2, 100.0)	85.7 (59.8, 100.0)
9 months	80.0 (55.2, 100.0)	NE (NE, NE)
12 months	80.0 (55.2, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	2 (20.0)	2 (28.6)
Number of Subjects Censored, n (%)	8 (80.0)	5 (71.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	1.64 (0.69, NE)
Median (95% CI)	NE (0.03, NE)	NE (0.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.7, 7.0*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.015 (1.229)
95% CI		(0.091, 11.292)
Log-rank p-value		0.936

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.8 (52.5, 100.0)	71.4 (38.0, 100.0)
6 months	78.8 (52.5, 100.0)	71.4 (38.0, 100.0)
9 months	78.8 (52.5, 100.0)	NE (NE, NE)
12 months	78.8 (52.5, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.48	4.57

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	1 (10.0)	0
Number of Subjects Censored, n (%)	9 (90.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.84, NE)	NE (NE, NE)
Median (95% CI)	NE (1.84, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.480

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (68.4, 100.0)	100.0 (100.0, 100.0)
6 months	88.9 (68.4, 100.0)	100.0 (100.0, 100.0)
9 months	88.9 (68.4, 100.0)	NE (NE, NE)
12 months	88.9 (68.4, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Vascular disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	2 (20.0)	1 (14.3)
Number of Subjects Censored, n (%)	8 (80.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	NE (0.62, NE)
Median (95% CI)	NE (0.03, NE)	NE (0.62, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.0*	0.6, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.081 (1.240)
95% CI		(0.095, 12.295)
Log-rank p-value		1.000

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Vascular disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.0 (55.2, 100.0)	85.7 (59.8, 100.0)
6 months	NE (NE, NE)	85.7 (59.8, 100.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.48	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	2 (20.0)	1 (14.3)
Number of Subjects Censored, n (%)	8 (80.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	NE (0.62, NE)
Median (95% CI)	NE (0.03, NE)	NE (0.62, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.0*	0.6, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.081 (1.240)
95% CI		(0.095, 12.295)
Log-rank p-value		1.000

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.0 (55.2, 100.0)	85.7 (59.8, 100.0)
6 months	NE (NE, NE)	85.7 (59.8, 100.0)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.48	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	4 (40.0)	0
Number of Subjects Censored, n (%)	6 (60.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.76 (0.49, NE)	NE (NE, NE)
Median (95% CI)	5.59 (0.49, NE)	NE (NE, NE)
75% percentile (95% CI)	5.59 (NE, NE)	NE (NE, NE)
Min, Max	0.5, 5.6	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.077

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	70.0 (41.6, 98.4)	100.0 (100.0, 100.0)
6 months	0.0 (NE, NE)	100.0 (100.0, 100.0)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.40	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	1 (10.0)	0
Number of Subjects Censored, n (%)	9 (90.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.66, NE)	NE (NE, NE)
Median (95% CI)	NE (0.66, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 13.0*	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.480

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (71.4, 100.0)	100.0 (100.0, 100.0)
6 months	90.0 (71.4, 100.0)	100.0 (100.0, 100.0)
9 months	90.0 (71.4, 100.0)	NE (NE, NE)
12 months	90.0 (71.4, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	3 (30.0)	0
Number of Subjects Censored, n (%)	7 (70.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (0.49, NE)	NE (NE, NE)
Median (95% CI)	5.59 (0.49, NE)	NE (NE, NE)
75% percentile (95% CI)	5.59 (NE, NE)	NE (NE, NE)
Min, Max	0.5, 5.6	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.117

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.0 (55.2, 100.0)	100.0 (100.0, 100.0)
6 months	0.0 (NE, NE)	100.0 (100.0, 100.0)
9 months	0.0 (NE, NE)	NE (NE, NE)
12 months	0.0 (NE, NE)	NE (NE, NE)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.48	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	0	2 (28.6)
Number of Subjects Censored, n (%)	10 (100.0)	5 (71.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.58 (0.26, NE)
Median (95% CI)	NE (NE, NE)	NE (0.26, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	0.3, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	71.4 (38.0, 100.0)
6 months	100.0 (100.0, 100.0)	71.4 (38.0, 100.0)
9 months	100.0 (100.0, 100.0)	NE (NE, NE)
12 months	100.0 (100.0, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	4.57

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	0	2 (28.6)
Number of Subjects Censored, n (%)	10 (100.0)	5 (71.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.58 (0.26, NE)
Median (95% CI)	NE (NE, NE)	NE (0.26, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	0.3, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	71.4 (38.0, 100.0)
6 months	100.0 (100.0, 100.0)	71.4 (38.0, 100.0)
9 months	100.0 (100.0, 100.0)	NE (NE, NE)
12 months	100.0 (100.0, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	4.57

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Nervous system disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	0	2 (28.6)
Number of Subjects Censored, n (%)	10 (100.0)	5 (71.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.38 (0.89, NE)
Median (95% CI)	NE (NE, NE)	NE (0.89, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (3.38, NE)
Min, Max	0.8*, 13.0*	0.9, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Nervous system disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	85.7 (59.8, 100.0)
6 months	100.0 (100.0, 100.0)	68.6 (32.1, 100.0)
9 months	100.0 (100.0, 100.0)	NE (NE, NE)
12 months	100.0 (100.0, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	4.57

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	0	1 (14.3)
Number of Subjects Censored, n (%)	10 (100.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.95, NE)
Median (95% CI)	NE (NE, NE)	NE (0.95, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	1.0, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	85.7 (59.8, 100.0)
6 months	100.0 (100.0, 100.0)	85.7 (59.8, 100.0)
9 months	100.0 (100.0, 100.0)	NE (NE, NE)
12 months	100.0 (100.0, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	3 (30.0)	2 (28.6)
Number of Subjects Censored, n (%)	7 (70.0)	5 (71.4)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.92, NE)	3.35 (0.95, NE)
Median (95% CI)	NE (0.92, NE)	NE (0.95, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (3.35, NE)
Min, Max	0.8*, 13.0*	1.0, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.227 (0.974)
95% CI		(0.182, 8.281)
Log-rank p-value		0.879

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	66.7 (35.9, 97.5)	85.7 (59.8, 100.0)
6 months	66.7 (35.9, 97.5)	68.6 (32.1, 100.0)
9 months	66.7 (35.9, 97.5)	NE (NE, NE)
12 months	66.7 (35.9, 97.5)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.28	4.57

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	3 (30.0)	1 (14.3)
Number of Subjects Censored, n (%)	7 (70.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.92, NE)	NE (3.35, NE)
Median (95% CI)	NE (0.92, NE)	NE (3.35, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.357 (1.186)
95% CI		(0.035, 3.646)
Log-rank p-value		0.493

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	66.7 (35.9, 97.5)	100.0 (100.0, 100.0)
6 months	66.7 (35.9, 97.5)	83.3 (53.5, 100.0)
9 months	66.7 (35.9, 97.5)	NE (NE, NE)
12 months	66.7 (35.9, 97.5)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.28	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Infections and infestations**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	2 (20.0)	1 (14.3)
Number of Subjects Censored, n (%)	8 (80.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.76, NE)	NE (0.66, NE)
Median (95% CI)	NE (0.76, NE)	NE (0.66, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8, 13.0*	0.7, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.438 (1.437)
95% CI		(0.146, 40.735)
Log-rank p-value		0.617

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Infections and infestations**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.8 (52.5, 100.0)	85.7 (59.8, 100.0)
6 months	78.8 (52.5, 100.0)	85.7 (59.8, 100.0)
9 months	78.8 (52.5, 100.0)	NE (NE, NE)
12 months	78.8 (52.5, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.58	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	1 (10.0)	0
Number of Subjects Censored, n (%)	9 (90.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.76, NE)	NE (NE, NE)
Median (95% CI)	NE (0.76, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8, 13.0*	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.480

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (71.4, 100.0)	100.0 (100.0, 100.0)
6 months	90.0 (71.4, 100.0)	100.0 (100.0, 100.0)
9 months	90.0 (71.4, 100.0)	NE (NE, NE)
12 months	90.0 (71.4, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	2 (20.0)	0
Number of Subjects Censored, n (%)	8 (80.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.02, NE)	NE (NE, NE)
Median (95% CI)	NE (1.02, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.362

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.2 (47.2, 100.0)	100.0 (100.0, 100.0)
6 months	76.2 (47.2, 100.0)	100.0 (100.0, 100.0)
9 months	76.2 (47.2, 100.0)	NE (NE, NE)
12 months	76.2 (47.2, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.48	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	2 (20.0)	0
Number of Subjects Censored, n (%)	8 (80.0)	7 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.02, NE)	NE (NE, NE)
Median (95% CI)	NE (1.02, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.362

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.2 (47.2, 100.0)	100.0 (100.0, 100.0)
6 months	76.2 (47.2, 100.0)	100.0 (100.0, 100.0)
9 months	76.2 (47.2, 100.0)	NE (NE, NE)
12 months	76.2 (47.2, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.48	5.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Psychiatric disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	0	1 (14.3)
Number of Subjects Censored, n (%)	10 (100.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.83, NE)
Median (95% CI)	NE (NE, NE)	NE (2.83, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	1.9*, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Psychiatric disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	83.3 (53.5, 100.0)
6 months	100.0 (100.0, 100.0)	83.3 (53.5, 100.0)
9 months	100.0 (100.0, 100.0)	NE (NE, NE)
12 months	100.0 (100.0, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Number of Subjects with Events, n (%)	0	1 (14.3)
Number of Subjects Censored, n (%)	10 (100.0)	6 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.72, NE)
Median (95% CI)	NE (NE, NE)	NE (0.72, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8*, 13.0*	0.7, 7.4*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
V600 E Mutation

Statistics	Placebo + BSC N=10	Fruquintinib + BSC N=7
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	85.7 (59.8, 100.0)
6 months	100.0 (100.0, 100.0)	85.7 (59.8, 100.0)
9 months	100.0 (100.0, 100.0)	NE (NE, NE)
12 months	100.0 (100.0, 100.0)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	4.67

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	9 (39.1)	36 (69.2)
Number of Subjects Censored, n (%)	14 (60.9)	16 (30.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.72 (0.07, NE)	0.28 (0.07, 0.66)
Median (95% CI)	NE (0.92, NE)	1.40 (0.66, 3.75)
75% percentile (95% CI)	NE (NE, NE)	6.97 (2.83, NE)
Min, Max	0.1, 6.4*	0.0, 10.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.480 (0.385)
95% CI		(1.165, 5.279)
Log-rank p-value		0.021

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	60.9 (40.9, 80.8)	38.1 (24.8, 51.4)
6 months	60.9 (40.9, 80.8)	25.4 (10.7, 40.1)
9 months	NE (NE, NE)	19.0 (3.6, 34.5)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.87	1.40

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	2 (8.7)	15 (28.8)
Number of Subjects Censored, n (%)	21 (91.3)	37 (71.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.07, NE)	1.58 (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.4*	0.1, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.786 (0.787)
95% CI		(1.022, 22.398)
Log-rank p-value		0.047

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (79.8, 100.0)	70.6 (58.0, 83.1)
6 months	91.3 (79.8, 100.0)	70.6 (58.0, 83.1)
9 months	NE (NE, NE)	70.6 (58.0, 83.1)
12 months	NE (NE, NE)	70.6 (58.0, 83.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.86	3.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	5 (21.7)	11 (21.2)
Number of Subjects Censored, n (%)	18 (78.3)	41 (78.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.36, NE)	6.97 (1.61, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 6.4*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.990 (0.595)
95% CI		(0.308, 3.176)
Log-rank p-value		0.816

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.3 (61.4, 95.1)	82.2 (71.5, 92.8)
6 months	78.3 (61.4, 95.1)	77.3 (63.8, 90.9)
9 months	NE (NE, NE)	71.4 (54.6, 88.2)
12 months	NE (NE, NE)	71.4 (54.6, 88.2)
18 months	NE (NE, NE)	71.4 (54.6, 88.2)
Median Follow-up Time (months)	2.83	3.43

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	1 (4.3)	1 (1.9)
Number of Subjects Censored, n (%)	22 (95.7)	51 (98.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.46, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.365 (1.509)
95% CI		(0.019, 7.032)
Log-rank p-value		0.745

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	98.0 (94.2, 100.0)
6 months	95.7 (87.3, 100.0)	98.0 (94.2, 100.0)
9 months	NE (NE, NE)	98.0 (94.2, 100.0)
12 months	NE (NE, NE)	98.0 (94.2, 100.0)
18 months	NE (NE, NE)	98.0 (94.2, 100.0)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	11 (21.2)
Number of Subjects Censored, n (%)	23 (100.0)	41 (78.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.28, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.015

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	79.9 (68.8, 91.1)
6 months	100.0 (100.0, 100.0)	76.5 (63.9, 89.0)
9 months	NE (NE, NE)	76.5 (63.9, 89.0)
12 months	NE (NE, NE)	76.5 (63.9, 89.0)
18 months	NE (NE, NE)	76.5 (63.9, 89.0)
Median Follow-up Time (months)	2.86	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	1 (4.3)	7 (13.5)
Number of Subjects Censored, n (%)	22 (95.7)	45 (86.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.27, NE)	12.22 (4.27, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (12.22, NE)
Min, Max	1.6*, 6.4*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.172 (1.181)
95% CI		(0.313, 32.122)
Log-rank p-value		0.447

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.7 (84.7, 100.0)	94.0 (87.5, 100.0)
6 months	94.7 (84.7, 100.0)	82.0 (67.9, 96.0)
9 months	NE (NE, NE)	82.0 (67.9, 96.0)
12 months	NE (NE, NE)	82.0 (67.9, 96.0)
18 months	NE (NE, NE)	61.5 (25.1, 97.8)
Median Follow-up Time (months)	2.86	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	1 (4.3)	5 (9.6)
Number of Subjects Censored, n (%)	22 (95.7)	47 (90.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.4*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.528 (1.098)
95% CI		(0.294, 21.757)
Log-rank p-value		0.418

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	90.1 (81.9, 98.4)
6 months	95.7 (87.3, 100.0)	90.1 (81.9, 98.4)
9 months	NE (NE, NE)	90.1 (81.9, 98.4)
12 months	NE (NE, NE)	90.1 (81.9, 98.4)
18 months	NE (NE, NE)	90.1 (81.9, 98.4)
Median Follow-up Time (months)	2.86	3.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	2 (3.8)
Number of Subjects Censored, n (%)	23 (100.0)	50 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.00, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.480

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.1 (94.3, 100.0)
6 months	100.0 (100.0, 100.0)	98.1 (94.3, 100.0)
9 months	NE (NE, NE)	98.1 (94.3, 100.0)
12 months	NE (NE, NE)	89.2 (72.2, 100.0)
18 months	NE (NE, NE)	89.2 (72.2, 100.0)
Median Follow-up Time (months)	2.86	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	2 (3.8)
Number of Subjects Censored, n (%)	23 (100.0)	50 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.371

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.1 (90.8, 100.0)
6 months	100.0 (100.0, 100.0)	96.1 (90.8, 100.0)
9 months	NE (NE, NE)	96.1 (90.8, 100.0)
12 months	NE (NE, NE)	96.1 (90.8, 100.0)
18 months	NE (NE, NE)	96.1 (90.8, 100.0)
Median Follow-up Time (months)	2.86	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	15 (65.2)	38 (73.1)
Number of Subjects Censored, n (%)	8 (34.8)	14 (26.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.66 (0.03, 1.02)	0.48 (0.26, 0.66)
Median (95% CI)	1.45 (0.69, NE)	0.82 (0.66, 2.69)
75% percentile (95% CI)	NE (1.61, NE)	4.50 (2.20, NE)
Min, Max	0.0, 6.4*	0.0, 10.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.157 (0.326)
95% CI		(0.611, 2.192)
Log-rank p-value		0.491

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	34.2 (14.6, 53.9)	32.7 (19.5, 45.8)
6 months	34.2 (14.6, 53.9)	22.4 (9.1, 35.7)
9 months	NE (NE, NE)	18.7 (5.8, 31.6)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.45	0.80

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	3 (13.0)	9 (17.3)
Number of Subjects Censored, n (%)	20 (87.0)	43 (82.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	6.47 (3.68, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.427 (0.723)
95% CI		(0.346, 5.891)
Log-rank p-value		0.550

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.5 (72.2, 100.0)	88.3 (79.6, 97.1)
6 months	86.5 (72.2, 100.0)	79.4 (65.0, 93.7)
9 months	NE (NE, NE)	73.7 (56.6, 90.8)
12 months	NE (NE, NE)	73.7 (56.6, 90.8)
18 months	NE (NE, NE)	73.7 (56.6, 90.8)
Median Follow-up Time (months)	2.83	3.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	3 (13.0)	6 (11.5)
Number of Subjects Censored, n (%)	20 (87.0)	46 (88.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.16, NE)	NE (9.00, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.529 (0.771)
95% CI		(0.117, 2.393)
Log-rank p-value		0.543

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.0 (73.2, 100.0)	90.4 (82.4, 98.4)
6 months	87.0 (73.2, 100.0)	90.4 (82.4, 98.4)
9 months	NE (NE, NE)	90.4 (82.4, 98.4)
12 months	NE (NE, NE)	81.3 (63.1, 99.6)
18 months	NE (NE, NE)	81.3 (63.1, 99.6)
Median Follow-up Time (months)	2.83	3.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	4 (17.4)	12 (23.1)
Number of Subjects Censored, n (%)	19 (82.6)	40 (76.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.10, NE)	12.25 (0.85, NE)
Median (95% CI)	NE (NE, NE)	NE (12.25, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (12.25, NE)
Min, Max	0.1, 6.4*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.352 (0.592)
95% CI		(0.424, 4.310)
Log-rank p-value		0.468

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.8 (65.6, 98.0)	78.3 (66.9, 89.7)
6 months	81.8 (65.6, 98.0)	78.3 (66.9, 89.7)
9 months	NE (NE, NE)	78.3 (66.9, 89.7)
12 months	NE (NE, NE)	78.3 (66.9, 89.7)
18 months	NE (NE, NE)	52.2 (9.8, 94.7)
Median Follow-up Time (months)	2.83	3.45

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	5 (21.7)	9 (17.3)
Number of Subjects Censored, n (%)	18 (78.3)	43 (82.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	NE (1.05, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.601 (0.608)
95% CI		(0.183, 1.976)
Log-rank p-value		0.489

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.7 (60.5, 95.0)	84.3 (74.3, 94.3)
6 months	77.7 (60.5, 95.0)	80.4 (68.4, 92.5)
9 months	NE (NE, NE)	80.4 (68.4, 92.5)
12 months	NE (NE, NE)	80.4 (68.4, 92.5)
18 months	NE (NE, NE)	80.4 (68.4, 92.5)
Median Follow-up Time (months)	2.83	3.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	1 (4.3)	9 (17.3)
Number of Subjects Censored, n (%)	22 (95.7)	43 (82.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	18.04 (1.87, NE)
Median (95% CI)	NE (NE, NE)	NE (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	1.0, 6.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.464 (1.063)
95% CI		(0.431, 27.828)
Log-rank p-value		0.244

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	86.2 (76.7, 95.7)
6 months	95.7 (87.3, 100.0)	82.9 (71.7, 94.0)
9 months	NE (NE, NE)	82.9 (71.7, 94.0)
12 months	NE (NE, NE)	82.9 (71.7, 94.0)
18 months	NE (NE, NE)	82.9 (71.7, 94.0)
Median Follow-up Time (months)	2.86	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	1 (4.3)	3 (5.8)
Number of Subjects Censored, n (%)	22 (95.7)	49 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.61, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6, 6.4*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.880 (1.405)
95% CI		(0.120, 29.532)
Log-rank p-value		0.371

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	93.9 (87.1, 100.0)
6 months	95.7 (87.3, 100.0)	93.9 (87.1, 100.0)
9 months	NE (NE, NE)	93.9 (87.1, 100.0)
12 months	NE (NE, NE)	93.9 (87.1, 100.0)
18 months	NE (NE, NE)	93.9 (87.1, 100.0)
Median Follow-up Time (months)	2.83	3.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	6 (11.5)
Number of Subjects Censored, n (%)	23 (100.0)	46 (88.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.50, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.114

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	89.9 (81.5, 98.3)
6 months	100.0 (100.0, 100.0)	85.2 (73.1, 97.2)
9 months	NE (NE, NE)	85.2 (73.1, 97.2)
12 months	NE (NE, NE)	85.2 (73.1, 97.2)
18 months	NE (NE, NE)	85.2 (73.1, 97.2)
Median Follow-up Time (months)	2.86	3.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	3 (5.8)
Number of Subjects Censored, n (%)	23 (100.0)	49 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.192

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.2 (87.8, 100.0)
6 months	100.0 (100.0, 100.0)	94.2 (87.8, 100.0)
9 months	NE (NE, NE)	94.2 (87.8, 100.0)
12 months	NE (NE, NE)	94.2 (87.8, 100.0)
18 months	NE (NE, NE)	94.2 (87.8, 100.0)
Median Follow-up Time (months)	2.86	3.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	2 (8.7)	0
Number of Subjects Censored, n (%)	21 (91.3)	52 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.53, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.070

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (79.8, 100.0)	100.0 (100.0, 100.0)
6 months	91.3 (79.8, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	5 (21.7)	19 (36.5)
Number of Subjects Censored, n (%)	18 (78.3)	33 (63.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	2.04 (0.95, 3.71)
Median (95% CI)	NE (NE, NE)	5.68 (3.68, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (5.68, NE)
Min, Max	0.0, 6.4*	0.0, 10.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.465 (0.556)
95% CI		(0.493, 4.360)
Log-rank p-value		0.565

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.3 (61.4, 95.1)	69.8 (56.9, 82.6)
6 months	78.3 (61.4, 95.1)	43.6 (20.2, 67.0)
9 months	NE (NE, NE)	43.6 (20.2, 67.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.96

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	12 (23.1)
Number of Subjects Censored, n (%)	23 (100.0)	40 (76.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.94 (1.45, NE)
Median (95% CI)	NE (NE, NE)	NE (6.97, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.038

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	82.4 (71.9, 92.8)
6 months	100.0 (100.0, 100.0)	74.5 (60.4, 88.5)
9 months	NE (NE, NE)	67.7 (49.7, 85.7)
12 months	NE (NE, NE)	67.7 (49.7, 85.7)
18 months	NE (NE, NE)	67.7 (49.7, 85.7)
Median Follow-up Time (months)	2.86	3.43

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	1 (4.3)	1 (1.9)
Number of Subjects Censored, n (%)	22 (95.7)	51 (98.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	NE (3.91, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.246 (1.566)
95% CI		(0.011, 5.295)
Log-rank p-value		0.480

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	100.0 (100.0, 100.0)
6 months	95.7 (87.3, 100.0)	96.0 (88.3, 100.0)
9 months	NE (NE, NE)	96.0 (88.3, 100.0)
12 months	NE (NE, NE)	96.0 (88.3, 100.0)
18 months	NE (NE, NE)	96.0 (88.3, 100.0)
Median Follow-up Time (months)	2.86	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	2 (3.8)
Number of Subjects Censored, n (%)	23 (100.0)	50 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.46, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.480

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.8 (93.6, 100.0)
6 months	100.0 (100.0, 100.0)	97.8 (93.6, 100.0)
9 months	NE (NE, NE)	90.8 (77.1, 100.0)
12 months	NE (NE, NE)	90.8 (77.1, 100.0)
18 months	NE (NE, NE)	90.8 (77.1, 100.0)
Median Follow-up Time (months)	2.86	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	2 (3.8)
Number of Subjects Censored, n (%)	23 (100.0)	50 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.51, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.414

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	100.0 (100.0, 100.0)	96.3 (89.2, 100.0)
9 months	NE (NE, NE)	87.5 (69.9, 100.0)
12 months	NE (NE, NE)	87.5 (69.9, 100.0)
18 months	NE (NE, NE)	87.5 (69.9, 100.0)
Median Follow-up Time (months)	2.86	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	1 (4.3)	0
Number of Subjects Censored, n (%)	22 (95.7)	52 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.53, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.110

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	100.0 (100.0, 100.0)
6 months	95.7 (87.3, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.86	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	4 (7.7)
Number of Subjects Censored, n (%)	23 (100.0)	48 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.68, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.334

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.0 (90.6, 100.0)
6 months	100.0 (100.0, 100.0)	91.0 (80.1, 100.0)
9 months	NE (NE, NE)	84.0 (67.4, 100.0)
12 months	NE (NE, NE)	84.0 (67.4, 100.0)
18 months	NE (NE, NE)	84.0 (67.4, 100.0)
Median Follow-up Time (months)	2.86	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	1 (4.3)	1 (1.9)
Number of Subjects Censored, n (%)	22 (95.7)	51 (98.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.43, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.618 (1.530)
95% CI		(0.031, 12.404)
Log-rank p-value		1.000

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	98.0 (94.2, 100.0)
6 months	95.7 (87.3, 100.0)	98.0 (94.2, 100.0)
9 months	NE (NE, NE)	98.0 (94.2, 100.0)
12 months	NE (NE, NE)	98.0 (94.2, 100.0)
18 months	NE (NE, NE)	98.0 (94.2, 100.0)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	1 (4.3)	2 (3.8)
Number of Subjects Censored, n (%)	22 (95.7)	50 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (8.51, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.441 (1.416)
95% CI		(0.027, 7.066)
Log-rank p-value		0.592

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	98.0 (94.1, 100.0)
6 months	95.7 (87.3, 100.0)	98.0 (94.1, 100.0)
9 months	NE (NE, NE)	89.8 (74.1, 100.0)
12 months	NE (NE, NE)	89.8 (74.1, 100.0)
18 months	NE (NE, NE)	89.8 (74.1, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	2 (3.8)
Number of Subjects Censored, n (%)	23 (100.0)	50 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.480

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.1 (90.8, 100.0)
6 months	100.0 (100.0, 100.0)	96.1 (90.8, 100.0)
9 months	NE (NE, NE)	96.1 (90.8, 100.0)
12 months	NE (NE, NE)	96.1 (90.8, 100.0)
18 months	NE (NE, NE)	96.1 (90.8, 100.0)
Median Follow-up Time (months)	2.86	3.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	1 (1.9)
Number of Subjects Censored, n (%)	23 (100.0)	51 (98.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.91, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.593

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	100.0 (100.0, 100.0)	96.0 (88.3, 100.0)
9 months	NE (NE, NE)	96.0 (88.3, 100.0)
12 months	NE (NE, NE)	96.0 (88.3, 100.0)
18 months	NE (NE, NE)	96.0 (88.3, 100.0)
Median Follow-up Time (months)	2.86	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	6 (26.1)	21 (40.4)
Number of Subjects Censored, n (%)	17 (73.9)	31 (59.6)
Time to first TEAE (months)		
25% percentile (95% CI)	1.61 (0.10, NE)	1.68 (0.92, 5.55)
Median (95% CI)	NE (NE, NE)	16.79 (4.67, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (16.79, NE)
Min, Max	0.1, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.098 (0.492)
95% CI		(0.418, 2.881)
Log-rank p-value		0.694

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.9 (56.0, 91.9)	68.3 (55.4, 81.2)
6 months	73.9 (56.0, 91.9)	55.9 (39.4, 72.4)
9 months	NE (NE, NE)	51.6 (34.3, 68.9)
12 months	NE (NE, NE)	51.6 (34.3, 68.9)
18 months	NE (NE, NE)	34.4 (4.6, 64.2)
Median Follow-up Time (months)	2.83	3.37

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	1 (4.3)	4 (7.7)
Number of Subjects Censored, n (%)	22 (95.7)	48 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.05, NE)	NE (6.87, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.1, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.028 (1.178)
95% CI		(0.102, 10.343)
Log-rank p-value		0.807

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	94.0 (87.5, 100.0)
6 months	95.7 (87.3, 100.0)	94.0 (87.5, 100.0)
9 months	NE (NE, NE)	87.8 (74.4, 100.0)
12 months	NE (NE, NE)	87.8 (74.4, 100.0)
18 months	NE (NE, NE)	87.8 (74.4, 100.0)
Median Follow-up Time (months)	2.86	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	1 (4.3)	5 (9.6)
Number of Subjects Censored, n (%)	22 (95.7)	47 (90.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.61, NE)	NE (5.55, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.913 (1.180)
95% CI		(0.090, 9.224)
Log-rank p-value		0.904

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	93.3 (86.0, 100.0)
6 months	95.7 (87.3, 100.0)	83.5 (69.0, 98.0)
9 months	NE (NE, NE)	83.5 (69.0, 98.0)
12 months	NE (NE, NE)	83.5 (69.0, 98.0)
18 months	NE (NE, NE)	83.5 (69.0, 98.0)
Median Follow-up Time (months)	2.86	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	1 (4.3)	3 (5.8)
Number of Subjects Censored, n (%)	22 (95.7)	49 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.968 (1.187)
95% CI		(0.095, 9.906)
Log-rank p-value		0.880

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	93.6 (86.5, 100.0)
6 months	95.7 (87.3, 100.0)	93.6 (86.5, 100.0)
9 months	NE (NE, NE)	93.6 (86.5, 100.0)
12 months	NE (NE, NE)	93.6 (86.5, 100.0)
18 months	NE (NE, NE)	93.6 (86.5, 100.0)
Median Follow-up Time (months)	2.86	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	1 (4.3)	2 (3.8)
Number of Subjects Censored, n (%)	22 (95.7)	50 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.056 (1.377)
95% CI		(0.071, 15.706)
Log-rank p-value		0.889

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	96.0 (90.7, 100.0)
6 months	95.7 (87.3, 100.0)	96.0 (90.7, 100.0)
9 months	NE (NE, NE)	96.0 (90.7, 100.0)
12 months	NE (NE, NE)	96.0 (90.7, 100.0)
18 months	NE (NE, NE)	96.0 (90.7, 100.0)
Median Follow-up Time (months)	2.86	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	3 (5.8)
Number of Subjects Censored, n (%)	23 (100.0)	49 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.223

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.1 (87.6, 100.0)
6 months	100.0 (100.0, 100.0)	94.1 (87.6, 100.0)
9 months	NE (NE, NE)	94.1 (87.6, 100.0)
12 months	NE (NE, NE)	94.1 (87.6, 100.0)
18 months	NE (NE, NE)	94.1 (87.6, 100.0)
Median Follow-up Time (months)	2.86	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	4 (7.7)
Number of Subjects Censored, n (%)	23 (100.0)	48 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.78, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.216

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.0 (87.4, 100.0)
6 months	100.0 (100.0, 100.0)	89.0 (77.7, 100.0)
9 months	NE (NE, NE)	89.0 (77.7, 100.0)
12 months	NE (NE, NE)	89.0 (77.7, 100.0)
18 months	NE (NE, NE)	89.0 (77.7, 100.0)
Median Follow-up Time (months)	2.86	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	3 (5.8)
Number of Subjects Censored, n (%)	23 (100.0)	49 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.254

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.1 (87.6, 100.0)
6 months	100.0 (100.0, 100.0)	94.1 (87.6, 100.0)
9 months	NE (NE, NE)	94.1 (87.6, 100.0)
12 months	NE (NE, NE)	94.1 (87.6, 100.0)
18 months	NE (NE, NE)	94.1 (87.6, 100.0)
Median Follow-up Time (months)	2.86	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	2 (3.8)
Number of Subjects Censored, n (%)	23 (100.0)	50 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.67, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.555

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.0 (94.0, 100.0)
6 months	100.0 (100.0, 100.0)	93.3 (83.6, 100.0)
9 months	NE (NE, NE)	93.3 (83.6, 100.0)
12 months	NE (NE, NE)	93.3 (83.6, 100.0)
18 months	NE (NE, NE)	93.3 (83.6, 100.0)
Median Follow-up Time (months)	2.86	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	9 (39.1)	17 (32.7)
Number of Subjects Censored, n (%)	14 (60.9)	35 (67.3)
Time to first TEAE (months)		
25% percentile (95% CI)	1.02 (0.03, NE)	0.92 (0.26, 9.69)
Median (95% CI)	NE (1.61, NE)	NE (7.56, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 3.7*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.800 (0.441)
95% CI		(0.337, 1.900)
Log-rank p-value		0.848

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	59.3 (38.4, 80.2)	72.9 (60.7, 85.0)
6 months	NE (NE, NE)	69.2 (55.8, 82.7)
9 months	NE (NE, NE)	61.5 (43.0, 80.1)
12 months	NE (NE, NE)	51.3 (27.3, 75.3)
18 months	NE (NE, NE)	51.3 (27.3, 75.3)
Median Follow-up Time (months)	2.27	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	2 (8.7)	7 (13.5)
Number of Subjects Censored, n (%)	21 (91.3)	45 (86.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.07, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.4*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.696 (0.829)
95% CI		(0.334, 8.610)
Log-rank p-value		0.311

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (79.8, 100.0)	86.5 (77.3, 95.8)
6 months	91.3 (79.8, 100.0)	86.5 (77.3, 95.8)
9 months	NE (NE, NE)	86.5 (77.3, 95.8)
12 months	NE (NE, NE)	86.5 (77.3, 95.8)
18 months	NE (NE, NE)	86.5 (77.3, 95.8)
Median Follow-up Time (months)	2.83	3.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	2 (8.7)	4 (7.7)
Number of Subjects Censored, n (%)	21 (91.3)	48 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.05, NE)	NE (10.28, NE)
Median (95% CI)	NE (NE, NE)	NE (10.28, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.1, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.079 (0.974)
95% CI		(0.160, 7.275)
Log-rank p-value		0.690

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (79.8, 100.0)	94.2 (87.7, 100.0)
6 months	91.3 (79.8, 100.0)	94.2 (87.7, 100.0)
9 months	NE (NE, NE)	94.2 (87.7, 100.0)
12 months	NE (NE, NE)	80.7 (55.7, 100.0)
18 months	NE (NE, NE)	80.7 (55.7, 100.0)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	3 (13.0)	2 (3.8)
Number of Subjects Censored, n (%)	20 (87.0)	50 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 4.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.278 (0.913)
95% CI		(0.046, 1.666)
Log-rank p-value		0.149

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.0 (73.2, 100.0)	96.2 (90.9, 100.0)
6 months	NE (NE, NE)	96.2 (90.9, 100.0)
9 months	NE (NE, NE)	96.2 (90.9, 100.0)
12 months	NE (NE, NE)	96.2 (90.9, 100.0)
18 months	NE (NE, NE)	96.2 (90.9, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	1 (4.3)	2 (3.8)
Number of Subjects Censored, n (%)	22 (95.7)	50 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.4*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.961 (1.227)
95% CI		(0.087, 10.645)
Log-rank p-value		0.991

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	96.1 (90.7, 100.0)
6 months	95.7 (87.3, 100.0)	96.1 (90.7, 100.0)
9 months	NE (NE, NE)	96.1 (90.7, 100.0)
12 months	NE (NE, NE)	96.1 (90.7, 100.0)
18 months	NE (NE, NE)	96.1 (90.7, 100.0)
Median Follow-up Time (months)	2.83	3.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Vascular disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	3 (13.0)	20 (38.5)
Number of Subjects Censored, n (%)	20 (87.0)	32 (61.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	0.72 (0.26, 3.25)
Median (95% CI)	NE (NE, NE)	NE (2.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 6.4*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.484 (0.622)
95% CI		(1.030, 11.783)
Log-rank p-value		0.048

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Vascular disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.0 (73.2, 100.0)	64.1 (50.7, 77.5)
6 months	87.0 (73.2, 100.0)	56.9 (41.6, 72.1)
9 months	NE (NE, NE)	56.9 (41.6, 72.1)
12 months	NE (NE, NE)	56.9 (41.6, 72.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	3 (13.0)	20 (38.5)
Number of Subjects Censored, n (%)	20 (87.0)	32 (61.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	0.72 (0.26, 3.25)
Median (95% CI)	NE (NE, NE)	NE (2.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 6.4*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.484 (0.622)
95% CI		(1.030, 11.783)
Log-rank p-value		0.048

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.0 (73.2, 100.0)	64.1 (50.7, 77.5)
6 months	87.0 (73.2, 100.0)	56.9 (41.6, 72.1)
9 months	NE (NE, NE)	56.9 (41.6, 72.1)
12 months	NE (NE, NE)	56.9 (41.6, 72.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	2 (8.7)	13 (25.0)
Number of Subjects Censored, n (%)	21 (91.3)	39 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.46, NE)	3.48 (0.76, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 6.4*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.582 (0.771)
95% CI		(0.570, 11.695)
Log-rank p-value		0.232

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (79.8, 100.0)	78.3 (66.9, 89.7)
6 months	91.3 (79.8, 100.0)	69.7 (54.5, 85.0)
9 months	NE (NE, NE)	69.7 (54.5, 85.0)
12 months	NE (NE, NE)	69.7 (54.5, 85.0)
18 months	NE (NE, NE)	69.7 (54.5, 85.0)
Median Follow-up Time (months)	2.83	2.96

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	2 (3.8)
Number of Subjects Censored, n (%)	23 (100.0)	50 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.70, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7*, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.460

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.0 (94.0, 100.0)
6 months	100.0 (100.0, 100.0)	93.1 (83.0, 100.0)
9 months	NE (NE, NE)	93.1 (83.0, 100.0)
12 months	NE (NE, NE)	93.1 (83.0, 100.0)
18 months	NE (NE, NE)	93.1 (83.0, 100.0)
Median Follow-up Time (months)	2.86	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	4 (7.7)
Number of Subjects Censored, n (%)	23 (100.0)	48 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.197

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	92.0 (84.5, 99.5)
6 months	100.0 (100.0, 100.0)	92.0 (84.5, 99.5)
9 months	NE (NE, NE)	92.0 (84.5, 99.5)
12 months	NE (NE, NE)	92.0 (84.5, 99.5)
18 months	NE (NE, NE)	92.0 (84.5, 99.5)
Median Follow-up Time (months)	2.86	3.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	1 (4.3)	3 (5.8)
Number of Subjects Censored, n (%)	22 (95.7)	49 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.91, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.563 (1.163)
95% CI		(0.160, 15.271)
Log-rank p-value		0.690

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.7 (84.7, 100.0)	94.1 (87.6, 100.0)
6 months	94.7 (84.7, 100.0)	94.1 (87.6, 100.0)
9 months	NE (NE, NE)	94.1 (87.6, 100.0)
12 months	NE (NE, NE)	94.1 (87.6, 100.0)
18 months	NE (NE, NE)	94.1 (87.6, 100.0)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	1 (4.3)	1 (1.9)
Number of Subjects Censored, n (%)	22 (95.7)	51 (98.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.46, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.391 (1.433)
95% CI		(0.024, 6.487)
Log-rank p-value		0.583

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	98.0 (94.2, 100.0)
6 months	95.7 (87.3, 100.0)	98.0 (94.2, 100.0)
9 months	NE (NE, NE)	98.0 (94.2, 100.0)
12 months	NE (NE, NE)	98.0 (94.2, 100.0)
18 months	NE (NE, NE)	98.0 (94.2, 100.0)
Median Follow-up Time (months)	2.86	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	2 (3.8)
Number of Subjects Censored, n (%)	23 (100.0)	50 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.70, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.480

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.1 (94.3, 100.0)
6 months	100.0 (100.0, 100.0)	98.1 (94.3, 100.0)
9 months	NE (NE, NE)	91.5 (78.7, 100.0)
12 months	NE (NE, NE)	91.5 (78.7, 100.0)
18 months	NE (NE, NE)	91.5 (78.7, 100.0)
Median Follow-up Time (months)	2.86	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	2 (3.8)
Number of Subjects Censored, n (%)	23 (100.0)	50 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.439

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.0 (90.6, 100.0)
6 months	100.0 (100.0, 100.0)	96.0 (90.6, 100.0)
9 months	NE (NE, NE)	96.0 (90.6, 100.0)
12 months	NE (NE, NE)	96.0 (90.6, 100.0)
18 months	NE (NE, NE)	96.0 (90.6, 100.0)
Median Follow-up Time (months)	2.86	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	4 (17.4)	13 (25.0)
Number of Subjects Censored, n (%)	19 (82.6)	39 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	6.24 (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (7.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 4.7*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.336 (0.608)
95% CI		(0.406, 4.398)
Log-rank p-value		0.514

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.6 (67.1, 98.1)	78.2 (66.7, 89.6)
6 months	NE (NE, NE)	78.2 (66.7, 89.6)
9 months	NE (NE, NE)	66.0 (47.6, 84.4)
12 months	NE (NE, NE)	66.0 (47.6, 84.4)
18 months	NE (NE, NE)	66.0 (47.6, 84.4)
Median Follow-up Time (months)	2.83	3.14

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	3 (13.0)	7 (13.5)
Number of Subjects Censored, n (%)	20 (87.0)	45 (86.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	NE (2.66, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 4.7*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.833 (0.748)
95% CI		(0.192, 3.609)
Log-rank p-value		0.937

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.0 (73.2, 100.0)	87.9 (78.8, 97.0)
6 months	NE (NE, NE)	87.9 (78.8, 97.0)
9 months	NE (NE, NE)	81.1 (65.9, 96.4)
12 months	NE (NE, NE)	81.1 (65.9, 96.4)
18 months	NE (NE, NE)	81.1 (65.9, 96.4)
Median Follow-up Time (months)	2.83	3.43

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	2 (8.7)	1 (1.9)
Number of Subjects Censored, n (%)	21 (91.3)	51 (98.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.89, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.225 (1.228)
95% CI		(0.020, 2.498)
Log-rank p-value		0.175

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (79.8, 100.0)	98.1 (94.3, 100.0)
6 months	91.3 (79.8, 100.0)	98.1 (94.3, 100.0)
9 months	NE (NE, NE)	98.1 (94.3, 100.0)
12 months	NE (NE, NE)	98.1 (94.3, 100.0)
18 months	NE (NE, NE)	98.1 (94.3, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	1 (1.9)
Number of Subjects Censored, n (%)	23 (100.0)	51 (98.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.1 (94.3, 100.0)
6 months	100.0 (100.0, 100.0)	98.1 (94.3, 100.0)
9 months	NE (NE, NE)	98.1 (94.3, 100.0)
12 months	NE (NE, NE)	98.1 (94.3, 100.0)
18 months	NE (NE, NE)	98.1 (94.3, 100.0)
Median Follow-up Time (months)	2.86	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Nervous system disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	2 (8.7)	11 (21.2)
Number of Subjects Censored, n (%)	21 (91.3)	41 (78.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	18.04 (1.51, NE)
Median (95% CI)	NE (NE, NE)	NE (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.6, 6.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.265 (0.778)
95% CI		(0.493, 10.396)
Log-rank p-value		0.249

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Nervous system disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (79.8, 100.0)	80.1 (69.0, 91.1)
6 months	91.3 (79.8, 100.0)	80.1 (69.0, 91.1)
9 months	NE (NE, NE)	80.1 (69.0, 91.1)
12 months	NE (NE, NE)	80.1 (69.0, 91.1)
18 months	NE (NE, NE)	80.1 (69.0, 91.1)
Median Follow-up Time (months)	2.83	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	1 (4.3)	3 (5.8)
Number of Subjects Censored, n (%)	22 (95.7)	49 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	18.04 (18.04, NE)
Median (95% CI)	NE (NE, NE)	NE (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.6, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.850 (1.259)
95% CI		(0.072, 10.022)
Log-rank p-value		0.930

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	96.0 (90.6, 100.0)
6 months	95.7 (87.3, 100.0)	96.0 (90.6, 100.0)
9 months	NE (NE, NE)	96.0 (90.6, 100.0)
12 months	NE (NE, NE)	96.0 (90.6, 100.0)
18 months	NE (NE, NE)	96.0 (90.6, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	1 (1.9)
Number of Subjects Censored, n (%)	23 (100.0)	51 (98.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.527

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.1 (94.3, 100.0)
6 months	100.0 (100.0, 100.0)	98.1 (94.3, 100.0)
9 months	NE (NE, NE)	98.1 (94.3, 100.0)
12 months	NE (NE, NE)	98.1 (94.3, 100.0)
18 months	NE (NE, NE)	98.1 (94.3, 100.0)
Median Follow-up Time (months)	2.86	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	2 (3.8)
Number of Subjects Censored, n (%)	23 (100.0)	50 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.332

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.8 (90.1, 100.0)
6 months	100.0 (100.0, 100.0)	95.8 (90.1, 100.0)
9 months	NE (NE, NE)	95.8 (90.1, 100.0)
12 months	NE (NE, NE)	95.8 (90.1, 100.0)
18 months	NE (NE, NE)	95.8 (90.1, 100.0)
Median Follow-up Time (months)	2.86	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	3 (13.0)	10 (19.2)
Number of Subjects Censored, n (%)	20 (87.0)	42 (80.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.79, NE)	6.54 (2.69, NE)
Median (95% CI)	NE (NE, NE)	NE (6.54, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.170 (0.682)
95% CI		(0.308, 4.452)
Log-rank p-value		0.924

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.0 (73.2, 100.0)	82.7 (71.6, 93.8)
6 months	87.0 (73.2, 100.0)	77.2 (62.5, 91.9)
9 months	NE (NE, NE)	70.7 (52.6, 88.8)
12 months	NE (NE, NE)	70.7 (52.6, 88.8)
18 months	NE (NE, NE)	70.7 (52.6, 88.8)
Median Follow-up Time (months)	2.83	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	1 (4.3)	8 (15.4)
Number of Subjects Censored, n (%)	22 (95.7)	44 (84.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (2.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.805 (1.068)
95% CI		(0.469, 30.854)
Log-rank p-value		0.202

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (87.3, 100.0)	82.7 (71.6, 93.8)
6 months	95.7 (87.3, 100.0)	82.7 (71.6, 93.8)
9 months	NE (NE, NE)	82.7 (71.6, 93.8)
12 months	NE (NE, NE)	82.7 (71.6, 93.8)
18 months	NE (NE, NE)	82.7 (71.6, 93.8)
Median Follow-up Time (months)	2.83	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	1 (1.9)
Number of Subjects Censored, n (%)	23 (100.0)	51 (98.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.532

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.0 (94.2, 100.0)
6 months	100.0 (100.0, 100.0)	98.0 (94.2, 100.0)
9 months	NE (NE, NE)	98.0 (94.2, 100.0)
12 months	NE (NE, NE)	98.0 (94.2, 100.0)
18 months	NE (NE, NE)	98.0 (94.2, 100.0)
Median Follow-up Time (months)	2.86	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Infections and infestations**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	1 (4.3)	12 (23.1)
Number of Subjects Censored, n (%)	22 (95.7)	40 (76.9)
Time to first TEAE (months)		
25% percentile (95% CI)	5.78 (NE, NE)	5.52 (2.50, NE)
Median (95% CI)	5.78 (NE, NE)	17.48 (7.69, NE)
75% percentile (95% CI)	5.78 (NE, NE)	NE (17.48, NE)
Min, Max	1.6*, 5.8	0.2, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.339 (1.111)
95% CI		(0.379, 29.447)
Log-rank p-value		0.209

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Infections and infestations**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	86.2 (76.7, 95.7)
6 months	0.0 (NE, NE)	74.2 (59.1, 89.3)
9 months	0.0 (NE, NE)	67.5 (48.8, 86.1)
12 months	0.0 (NE, NE)	67.5 (48.8, 86.1)
18 months	0.0 (NE, NE)	45.0 (6.9, 83.1)
Median Follow-up Time (months)	2.86	3.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	3 (5.8)
Number of Subjects Censored, n (%)	23 (100.0)	49 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.52, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.460

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.0 (94.0, 100.0)
6 months	100.0 (100.0, 100.0)	89.1 (76.7, 100.0)
9 months	NE (NE, NE)	89.1 (76.7, 100.0)
12 months	NE (NE, NE)	89.1 (76.7, 100.0)
18 months	NE (NE, NE)	89.1 (76.7, 100.0)
Median Follow-up Time (months)	2.86	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	3 (5.8)
Number of Subjects Censored, n (%)	23 (100.0)	49 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.156

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.1 (87.6, 100.0)
6 months	100.0 (100.0, 100.0)	94.1 (87.6, 100.0)
9 months	NE (NE, NE)	94.1 (87.6, 100.0)
12 months	NE (NE, NE)	94.1 (87.6, 100.0)
18 months	NE (NE, NE)	94.1 (87.6, 100.0)
Median Follow-up Time (months)	2.86	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	3 (13.0)	8 (15.4)
Number of Subjects Censored, n (%)	20 (87.0)	44 (84.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (2.63, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.4*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.383 (0.708)
95% CI		(0.345, 5.543)
Log-rank p-value		0.862

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.0 (73.2, 100.0)	86.1 (76.6, 95.7)
6 months	87.0 (73.2, 100.0)	82.8 (71.6, 94.0)
9 months	NE (NE, NE)	82.8 (71.6, 94.0)
12 months	NE (NE, NE)	82.8 (71.6, 94.0)
18 months	NE (NE, NE)	82.8 (71.6, 94.0)
Median Follow-up Time (months)	2.83	3.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	3 (13.0)	4 (7.7)
Number of Subjects Censored, n (%)	20 (87.0)	48 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	17.74 (17.74, NE)
Median (95% CI)	NE (NE, NE)	NE (17.74, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.74, NE)
Min, Max	0.7, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.323 (0.840)
95% CI		(0.062, 1.673)
Log-rank p-value		0.116

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.0 (73.2, 100.0)	96.0 (90.6, 100.0)
6 months	87.0 (73.2, 100.0)	92.7 (84.4, 100.0)
9 months	NE (NE, NE)	92.7 (84.4, 100.0)
12 months	NE (NE, NE)	92.7 (84.4, 100.0)
18 months	NE (NE, NE)	61.8 (12.0, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	6 (11.5)
Number of Subjects Censored, n (%)	23 (100.0)	46 (88.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.076

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	88.1 (79.2, 97.1)
6 months	100.0 (100.0, 100.0)	88.1 (79.2, 97.1)
9 months	NE (NE, NE)	88.1 (79.2, 97.1)
12 months	NE (NE, NE)	88.1 (79.2, 97.1)
18 months	NE (NE, NE)	88.1 (79.2, 97.1)
Median Follow-up Time (months)	2.86	3.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Endocrine disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	14 (26.9)
Number of Subjects Censored, n (%)	23 (100.0)	38 (73.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.07 (2.07, 9.33)
Median (95% CI)	NE (NE, NE)	NE (4.37, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7*, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.033

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Endocrine disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	83.3 (72.7, 93.9)
6 months	100.0 (100.0, 100.0)	61.9 (43.7, 80.1)
9 months	NE (NE, NE)	61.9 (43.7, 80.1)
12 months	NE (NE, NE)	51.6 (27.7, 75.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.86	3.37

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	13 (25.0)
Number of Subjects Censored, n (%)	23 (100.0)	39 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.07 (2.53, 9.33)
Median (95% CI)	NE (NE, NE)	NE (4.37, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7*, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.059

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	85.3 (75.2, 95.4)
6 months	100.0 (100.0, 100.0)	69.1 (52.5, 85.7)
9 months	NE (NE, NE)	61.4 (40.9, 81.9)
12 months	NE (NE, NE)	52.6 (28.9, 76.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.86	3.40

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	3 (13.0)	9 (17.3)
Number of Subjects Censored, n (%)	20 (87.0)	43 (82.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	NE (2.66, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.300 (0.732)
95% CI		(0.310, 5.455)
Log-rank p-value		0.925

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.0 (73.2, 100.0)	83.7 (73.4, 94.1)
6 months	87.0 (73.2, 100.0)	80.4 (68.5, 92.2)
9 months	NE (NE, NE)	80.4 (68.5, 92.2)
12 months	NE (NE, NE)	80.4 (68.5, 92.2)
18 months	NE (NE, NE)	80.4 (68.5, 92.2)
Median Follow-up Time (months)	2.83	3.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	3 (13.0)	4 (7.7)
Number of Subjects Censored, n (%)	20 (87.0)	48 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.490 (0.879)
95% CI		(0.088, 2.741)
Log-rank p-value		0.302

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.0 (73.2, 100.0)	91.7 (83.9, 99.5)
6 months	87.0 (73.2, 100.0)	91.7 (83.9, 99.5)
9 months	NE (NE, NE)	91.7 (83.9, 99.5)
12 months	NE (NE, NE)	91.7 (83.9, 99.5)
18 months	NE (NE, NE)	91.7 (83.9, 99.5)
Median Follow-up Time (months)	2.83	3.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	1 (1.9)
Number of Subjects Censored, n (%)	23 (100.0)	51 (98.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.439

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.1 (94.3, 100.0)
6 months	100.0 (100.0, 100.0)	98.1 (94.3, 100.0)
9 months	NE (NE, NE)	98.1 (94.3, 100.0)
12 months	NE (NE, NE)	98.1 (94.3, 100.0)
18 months	NE (NE, NE)	98.1 (94.3, 100.0)
Median Follow-up Time (months)	2.86	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	4 (7.7)
Number of Subjects Censored, n (%)	23 (100.0)	48 (92.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.251

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.8 (87.0, 100.0)
6 months	100.0 (100.0, 100.0)	90.3 (81.0, 99.7)
9 months	NE (NE, NE)	90.3 (81.0, 99.7)
12 months	NE (NE, NE)	90.3 (81.0, 99.7)
18 months	NE (NE, NE)	90.3 (81.0, 99.7)
Median Follow-up Time (months)	2.86	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	2 (8.7)	5 (9.6)
Number of Subjects Censored, n (%)	21 (91.3)	47 (90.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.92, NE)	NE (5.55, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9, 6.4*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.654 (1.064)
95% CI		(0.081, 5.265)
Log-rank p-value		0.989

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (79.8, 100.0)	96.2 (90.9, 100.0)
6 months	91.3 (79.8, 100.0)	87.6 (75.2, 100.0)
9 months	NE (NE, NE)	80.9 (63.8, 98.0)
12 months	NE (NE, NE)	80.9 (63.8, 98.0)
18 months	NE (NE, NE)	80.9 (63.8, 98.0)
Median Follow-up Time (months)	2.86	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Number of Subjects with Events, n (%)	0	3 (5.8)
Number of Subjects Censored, n (%)	23 (100.0)	49 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.55, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6*, 6.4*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.480

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3I
Summary of Time to Onset of TEAE by SOC/PT by BRAF Status
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Other

Statistics	Placebo + BSC N=23	Fruquintinib + BSC N=52
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.1 (94.3, 100.0)
6 months	100.0 (100.0, 100.0)	92.9 (82.5, 100.0)
9 months	NE (NE, NE)	85.8 (69.2, 100.0)
12 months	NE (NE, NE)	85.8 (69.2, 100.0)
18 months	NE (NE, NE)	85.8 (69.2, 100.0)
Median Follow-up Time (months)	2.86	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	19 (42.2)	41 (53.9)
Number of Subjects Censored, n (%)	26 (57.8)	35 (46.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.72 (0.36, 1.87)	0.71 (0.26, 1.05)
Median (95% CI)	NE (1.87, NE)	2.79 (1.12, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.1, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.389 (0.287)
95% CI		(0.791, 2.439)
Log-rank p-value		0.331

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	56.5 (41.7, 71.4)	49.6 (38.2, 60.9)
6 months	NE (NE, NE)	42.1 (29.7, 54.6)
9 months	NE (NE, NE)	42.1 (29.7, 54.6)
12 months	NE (NE, NE)	42.1 (29.7, 54.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.94	1.91

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	8 (17.8)	18 (23.7)
Number of Subjects Censored, n (%)	37 (82.2)	58 (76.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.72, NE)	NE (1.05, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.3, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.379 (0.438)
95% CI		(0.585, 3.255)
Log-rank p-value		0.526

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.8 (70.4, 93.3)	75.3 (65.3, 85.2)
6 months	NE (NE, NE)	75.3 (65.3, 85.2)
9 months	NE (NE, NE)	75.3 (65.3, 85.2)
12 months	NE (NE, NE)	75.3 (65.3, 85.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	7 (15.6)	12 (15.8)
Number of Subjects Censored, n (%)	38 (84.4)	64 (84.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.35, NE)	NE (1.84, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.899 (0.489)
95% CI		(0.344, 2.346)
Log-rank p-value		0.886

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.1 (73.2, 94.9)	85.2 (77.2, 93.3)
6 months	NE (NE, NE)	82.4 (72.9, 91.9)
9 months	NE (NE, NE)	82.4 (72.9, 91.9)
12 months	NE (NE, NE)	82.4 (72.9, 91.9)
18 months	NE (NE, NE)	82.4 (72.9, 91.9)
Median Follow-up Time (months)	2.83	3.47

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	4 (8.9)	4 (5.3)
Number of Subjects Censored, n (%)	41 (91.1)	72 (94.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.778 (0.720)
95% CI		(0.190, 3.189)
Log-rank p-value		0.803

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.1 (80.7, 99.4)	94.7 (89.7, 99.8)
6 months	NE (NE, NE)	94.7 (89.7, 99.8)
9 months	NE (NE, NE)	94.7 (89.7, 99.8)
12 months	NE (NE, NE)	94.7 (89.7, 99.8)
18 months	NE (NE, NE)	94.7 (89.7, 99.8)
Median Follow-up Time (months)	2.83	3.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	1 (2.2)	10 (13.2)
Number of Subjects Censored, n (%)	44 (97.8)	66 (86.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.26, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.310 (1.059)
95% CI		(0.792, 50.257)
Log-rank p-value		0.037

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (93.5, 100.0)	89.4 (82.5, 96.4)
6 months	NE (NE, NE)	86.9 (78.5, 95.2)
9 months	NE (NE, NE)	80.7 (66.6, 94.7)
12 months	NE (NE, NE)	80.7 (66.6, 94.7)
18 months	NE (NE, NE)	80.7 (66.6, 94.7)
Median Follow-up Time (months)	2.83	3.40

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	3 (6.7)	5 (6.6)
Number of Subjects Censored, n (%)	42 (93.3)	71 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.266 (0.754)
95% CI		(0.289, 5.543)
Log-rank p-value		0.814

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.4 (84.2, 100.0)	93.4 (87.7, 99.0)
6 months	NE (NE, NE)	93.4 (87.7, 99.0)
9 months	NE (NE, NE)	93.4 (87.7, 99.0)
12 months	NE (NE, NE)	93.4 (87.7, 99.0)
18 months	NE (NE, NE)	93.4 (87.7, 99.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	2 (4.4)	2 (2.6)
Number of Subjects Censored, n (%)	43 (95.6)	74 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 5.6*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.816 (1.000)
95% CI		(0.115, 5.796)
Log-rank p-value		0.839

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.7 (87.5, 100.0)	97.4 (93.8, 100.0)
6 months	NE (NE, NE)	97.4 (93.8, 100.0)
9 months	NE (NE, NE)	97.4 (93.8, 100.0)
12 months	NE (NE, NE)	97.4 (93.8, 100.0)
18 months	NE (NE, NE)	97.4 (93.8, 100.0)
Median Follow-up Time (months)	2.83	3.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	1 (2.2)	3 (3.9)
Number of Subjects Censored, n (%)	44 (97.8)	73 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.05, NE)
Median (95% CI)	NE (NE, NE)	NE (9.82, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.000 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.046

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (92.3, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	93.3 (80.7, 100.0)
12 months	NE (NE, NE)	76.0 (51.9, 100.0)
18 months	NE (NE, NE)	76.0 (51.9, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	1 (1.3)
Number of Subjects Censored, n (%)	45 (100.0)	75 (98.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.75, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	93.3 (80.7, 100.0)
12 months	NE (NE, NE)	93.3 (80.7, 100.0)
18 months	NE (NE, NE)	93.3 (80.7, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	2 (2.6)
Number of Subjects Censored, n (%)	45 (100.0)	74 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.57, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.361

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.7 (96.1, 100.0)
6 months	NE (NE, NE)	98.7 (96.1, 100.0)
9 months	NE (NE, NE)	91.1 (76.6, 100.0)
12 months	NE (NE, NE)	91.1 (76.6, 100.0)
18 months	NE (NE, NE)	91.1 (76.6, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	26 (57.8)	47 (61.8)
Number of Subjects Censored, n (%)	19 (42.2)	29 (38.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.46 (0.07, 0.69)	0.69 (0.46, 0.72)
Median (95% CI)	1.58 (0.69, NE)	2.27 (0.92, 4.70)
75% percentile (95% CI)	NE (NE, NE)	7.75 (4.70, NE)
Min, Max	0.0, 5.6*	0.0, 10.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.795 (0.258)
95% CI		(0.480, 1.317)
Log-rank p-value		0.548

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	41.6 (27.1, 56.2)	47.9 (36.5, 59.3)
6 months	NE (NE, NE)	32.3 (18.4, 46.3)
9 months	NE (NE, NE)	8.6 (0.0, 23.4)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.41	1.69

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	6 (13.3)	11 (14.5)
Number of Subjects Censored, n (%)	39 (86.7)	65 (85.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (3.88, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.017 (0.528)
95% CI		(0.361, 2.862)
Log-rank p-value		0.979

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.7 (76.7, 96.6)	89.4 (82.5, 96.4)
6 months	NE (NE, NE)	83.5 (73.3, 93.8)
9 months	NE (NE, NE)	78.3 (64.5, 92.1)
12 months	NE (NE, NE)	78.3 (64.5, 92.1)
18 months	NE (NE, NE)	78.3 (64.5, 92.1)
Median Follow-up Time (months)	2.83	3.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	10 (22.2)	6 (7.9)
Number of Subjects Censored, n (%)	35 (77.8)	70 (92.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.59, NE)	NE (9.00, NE)
Median (95% CI)	NE (NE, NE)	NE (9.20, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.185 (0.623)
95% CI		(0.055, 0.627)
Log-rank p-value		0.006

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.5 (65.2, 89.8)	94.6 (89.4, 99.8)
6 months	NE (NE, NE)	94.6 (89.4, 99.8)
9 months	NE (NE, NE)	94.6 (89.4, 99.8)
12 months	NE (NE, NE)	78.0 (56.7, 99.4)
18 months	NE (NE, NE)	78.0 (56.7, 99.4)
Median Follow-up Time (months)	2.79	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	7 (15.6)	14 (18.4)
Number of Subjects Censored, n (%)	38 (84.4)	62 (81.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.61, NE)	7.75 (3.68, NE)
Median (95% CI)	NE (NE, NE)	12.25 (9.23, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (12.25, NE)
Min, Max	0.0, 5.6*	0.2, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.578 (0.531)
95% CI		(0.204, 1.637)
Log-rank p-value		0.449

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.9 (73.0, 94.9)	87.8 (80.2, 95.3)
6 months	NE (NE, NE)	85.2 (76.3, 94.0)
9 months	NE (NE, NE)	73.5 (56.4, 90.6)
12 months	NE (NE, NE)	65.3 (43.9, 86.7)
18 months	NE (NE, NE)	49.0 (17.0, 81.0)
Median Follow-up Time (months)	2.83	3.33

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	4 (8.9)	8 (10.5)
Number of Subjects Censored, n (%)	41 (91.1)	68 (89.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.70, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.830 (0.643)
95% CI		(0.235, 2.923)
Log-rank p-value		0.825

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.1 (82.8, 99.4)	91.5 (84.9, 98.0)
6 months	NE (NE, NE)	83.5 (71.4, 95.7)
9 months	NE (NE, NE)	83.5 (71.4, 95.7)
12 months	NE (NE, NE)	83.5 (71.4, 95.7)
18 months	NE (NE, NE)	83.5 (71.4, 95.7)
Median Follow-up Time (months)	2.83	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	7 (15.6)	6 (7.9)
Number of Subjects Censored, n (%)	38 (84.4)	70 (92.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.58, NE)	NE (7.10, NE)
Median (95% CI)	NE (NE, NE)	NE (9.20, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 5.6*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.257 (0.700)
95% CI		(0.065, 1.013)
Log-rank p-value		0.055

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.2 (73.5, 95.0)	96.0 (91.6, 100.0)
6 months	NE (NE, NE)	93.5 (87.0, 100.0)
9 months	NE (NE, NE)	87.3 (74.0, 100.0)
12 months	NE (NE, NE)	78.5 (58.4, 98.7)
18 months	NE (NE, NE)	78.5 (58.4, 98.7)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	1 (2.2)	8 (10.5)
Number of Subjects Censored, n (%)	44 (97.8)	68 (89.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.87, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.878 (1.073)
95% CI		(0.474, 31.737)
Log-rank p-value		0.221

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (93.0, 100.0)	90.7 (84.1, 97.3)
6 months	NE (NE, NE)	90.7 (84.1, 97.3)
9 months	NE (NE, NE)	85.0 (72.6, 97.4)
12 months	NE (NE, NE)	85.0 (72.6, 97.4)
18 months	NE (NE, NE)	85.0 (72.6, 97.4)
Median Follow-up Time (months)	2.83	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	2 (4.4)	8 (10.5)
Number of Subjects Censored, n (%)	43 (95.6)	68 (89.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.79, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.350 (0.807)
95% CI		(0.483, 11.425)
Log-rank p-value		0.291

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (89.5, 100.0)	90.2 (83.2, 97.1)
6 months	NE (NE, NE)	90.2 (83.2, 97.1)
9 months	NE (NE, NE)	82.7 (67.2, 98.1)
12 months	NE (NE, NE)	82.7 (67.2, 98.1)
18 months	NE (NE, NE)	82.7 (67.2, 98.1)
Median Follow-up Time (months)	2.83	3.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	1 (2.2)	1 (1.3)
Number of Subjects Censored, n (%)	44 (97.8)	75 (98.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.795 (1.415)
95% CI		(0.050, 12.721)
Log-rank p-value		0.871

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (93.5, 100.0)	98.6 (96.0, 100.0)
6 months	NE (NE, NE)	98.6 (96.0, 100.0)
9 months	NE (NE, NE)	98.6 (96.0, 100.0)
12 months	NE (NE, NE)	98.6 (96.0, 100.0)
18 months	NE (NE, NE)	98.6 (96.0, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	1 (2.2)	1 (1.3)
Number of Subjects Censored, n (%)	44 (97.8)	75 (98.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.887 (1.555)
95% CI		(0.042, 18.707)
Log-rank p-value		0.954

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (92.3, 100.0)	98.7 (96.1, 100.0)
6 months	NE (NE, NE)	98.7 (96.1, 100.0)
9 months	NE (NE, NE)	98.7 (96.1, 100.0)
12 months	NE (NE, NE)	98.7 (96.1, 100.0)
18 months	NE (NE, NE)	98.7 (96.1, 100.0)
Median Follow-up Time (months)	2.83	3.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	2 (4.4)	0
Number of Subjects Censored, n (%)	43 (95.6)	76 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.070

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (89.2, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	10 (22.2)	27 (35.5)
Number of Subjects Censored, n (%)	35 (77.8)	49 (64.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	2.04 (0.95, 3.71)
Median (95% CI)	NE (NE, NE)	8.02 (3.71, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.1, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.595 (0.381)
95% CI		(0.757, 3.364)
Log-rank p-value		0.165

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.7 (65.5, 89.9)	69.3 (58.4, 80.1)
6 months	NE (NE, NE)	57.6 (43.2, 71.9)
9 months	NE (NE, NE)	49.3 (30.0, 68.6)
12 months	NE (NE, NE)	49.3 (30.0, 68.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	6 (13.3)	10 (13.2)
Number of Subjects Censored, n (%)	39 (86.7)	66 (86.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.14, NE)	NE (3.71, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.145 (0.529)
95% CI		(0.406, 3.230)
Log-rank p-value		0.799

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.2 (75.9, 96.5)	87.4 (79.6, 95.1)
6 months	NE (NE, NE)	84.8 (75.8, 93.8)
9 months	NE (NE, NE)	84.8 (75.8, 93.8)
12 months	NE (NE, NE)	84.8 (75.8, 93.8)
18 months	NE (NE, NE)	84.8 (75.8, 93.8)
Median Follow-up Time (months)	2.83	3.33

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	3 (3.9)
Number of Subjects Censored, n (%)	45 (100.0)	73 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.02, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.214

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.2 (93.3, 100.0)
6 months	NE (NE, NE)	97.2 (93.3, 100.0)
9 months	NE (NE, NE)	90.7 (77.9, 100.0)
12 months	NE (NE, NE)	90.7 (77.9, 100.0)
18 months	NE (NE, NE)	90.7 (77.9, 100.0)
Median Follow-up Time (months)	2.83	3.47

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	3 (3.9)
Number of Subjects Censored, n (%)	45 (100.0)	73 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.192

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.0 (91.5, 100.0)
6 months	NE (NE, NE)	96.0 (91.5, 100.0)
9 months	NE (NE, NE)	96.0 (91.5, 100.0)
12 months	NE (NE, NE)	96.0 (91.5, 100.0)
18 months	NE (NE, NE)	96.0 (91.5, 100.0)
Median Follow-up Time (months)	2.83	3.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	4 (5.3)
Number of Subjects Censored, n (%)	45 (100.0)	72 (94.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.51, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.248

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.2 (93.3, 100.0)
6 months	NE (NE, NE)	94.6 (88.4, 100.0)
9 months	NE (NE, NE)	86.0 (69.0, 100.0)
12 months	NE (NE, NE)	86.0 (69.0, 100.0)
18 months	NE (NE, NE)	86.0 (69.0, 100.0)
Median Follow-up Time (months)	2.83	3.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	1 (2.2)	4 (5.3)
Number of Subjects Censored, n (%)	44 (97.8)	72 (94.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 5.6*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.104 (1.145)
95% CI		(0.223, 19.835)
Log-rank p-value		0.419

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (93.5, 100.0)	96.1 (91.7, 100.0)
6 months	NE (NE, NE)	92.1 (83.3, 100.0)
9 months	NE (NE, NE)	92.1 (83.3, 100.0)
12 months	NE (NE, NE)	92.1 (83.3, 100.0)
18 months	NE (NE, NE)	92.1 (83.3, 100.0)
Median Follow-up Time (months)	2.83	3.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	4 (5.3)
Number of Subjects Censored, n (%)	45 (100.0)	72 (94.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.10, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.146

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.9 (91.4, 100.0)
6 months	NE (NE, NE)	95.9 (91.4, 100.0)
9 months	NE (NE, NE)	89.5 (76.7, 100.0)
12 months	NE (NE, NE)	89.5 (76.7, 100.0)
18 months	NE (NE, NE)	89.5 (76.7, 100.0)
Median Follow-up Time (months)	2.83	3.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	2 (2.6)
Number of Subjects Censored, n (%)	45 (100.0)	74 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.273

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.2 (93.5, 100.0)
6 months	NE (NE, NE)	97.2 (93.5, 100.0)
9 months	NE (NE, NE)	97.2 (93.5, 100.0)
12 months	NE (NE, NE)	97.2 (93.5, 100.0)
18 months	NE (NE, NE)	97.2 (93.5, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	4 (5.3)
Number of Subjects Censored, n (%)	45 (100.0)	72 (94.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.51, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.218

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.3 (93.7, 100.0)
6 months	NE (NE, NE)	95.2 (89.8, 100.0)
9 months	NE (NE, NE)	87.3 (71.6, 100.0)
12 months	NE (NE, NE)	87.3 (71.6, 100.0)
18 months	NE (NE, NE)	87.3 (71.6, 100.0)
Median Follow-up Time (months)	2.83	3.40

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	1 (2.2)	0
Number of Subjects Censored, n (%)	44 (97.8)	76 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.145

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (93.5, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	1 (2.2)	0
Number of Subjects Censored, n (%)	44 (97.8)	76 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.270

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (93.0, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	7 (15.6)	28 (36.8)
Number of Subjects Censored, n (%)	38 (84.4)	48 (63.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.94, NE)	1.58 (0.69, 3.68)
Median (95% CI)	NE (NE, NE)	16.79 (3.94, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (16.79, NE)
Min, Max	0.6, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.367 (0.435)
95% CI		(1.009, 5.552)
Log-rank p-value		0.035

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.6 (70.6, 94.7)	67.1 (56.2, 78.0)
6 months	NE (NE, NE)	58.4 (44.9, 71.8)
9 months	NE (NE, NE)	58.4 (44.9, 71.8)
12 months	NE (NE, NE)	58.4 (44.9, 71.8)
18 months	NE (NE, NE)	29.2 (0.0, 70.2)
Median Follow-up Time (months)	2.83	2.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	3 (6.7)	10 (13.2)
Number of Subjects Censored, n (%)	42 (93.3)	66 (86.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.83, NE)	NE (6.87, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.819 (0.690)
95% CI		(0.471, 7.029)
Log-rank p-value		0.306

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.2 (81.5, 100.0)	89.2 (82.2, 96.3)
6 months	NE (NE, NE)	86.7 (78.2, 95.1)
9 months	NE (NE, NE)	81.3 (68.3, 94.2)
12 months	NE (NE, NE)	81.3 (68.3, 94.2)
18 months	NE (NE, NE)	81.3 (68.3, 94.2)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	2 (4.4)	11 (14.5)
Number of Subjects Censored, n (%)	43 (95.6)	65 (85.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.98, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.783 (0.788)
95% CI		(0.594, 13.051)
Log-rank p-value		0.163

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (89.5, 100.0)	88.0 (80.6, 95.3)
6 months	NE (NE, NE)	81.2 (69.8, 92.7)
9 months	NE (NE, NE)	81.2 (69.8, 92.7)
12 months	NE (NE, NE)	81.2 (69.8, 92.7)
18 months	NE (NE, NE)	81.2 (69.8, 92.7)
Median Follow-up Time (months)	2.83	3.40

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	1 (2.2)	9 (11.8)
Number of Subjects Censored, n (%)	44 (97.8)	67 (88.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.98, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.227 (1.071)
95% CI		(0.641, 42.645)
Log-rank p-value		0.089

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (93.5, 100.0)	89.0 (81.7, 96.2)
6 months	NE (NE, NE)	86.3 (77.5, 95.0)
9 months	NE (NE, NE)	86.3 (77.5, 95.0)
12 months	NE (NE, NE)	86.3 (77.5, 95.0)
18 months	NE (NE, NE)	86.3 (77.5, 95.0)
Median Follow-up Time (months)	2.83	3.47

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	5 (6.6)
Number of Subjects Censored, n (%)	45 (100.0)	71 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.050

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.4 (89.0, 99.7)
6 months	NE (NE, NE)	91.8 (84.7, 99.0)
9 months	NE (NE, NE)	91.8 (84.7, 99.0)
12 months	NE (NE, NE)	91.8 (84.7, 99.0)
18 months	NE (NE, NE)	91.8 (84.7, 99.0)
Median Follow-up Time (months)	2.83	3.47

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	1 (1.3)
Number of Subjects Censored, n (%)	45 (100.0)	75 (98.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.386

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.5 (95.5, 100.0)
6 months	NE (NE, NE)	98.5 (95.5, 100.0)
9 months	NE (NE, NE)	98.5 (95.5, 100.0)
12 months	NE (NE, NE)	98.5 (95.5, 100.0)
18 months	NE (NE, NE)	98.5 (95.5, 100.0)
Median Follow-up Time (months)	2.83	3.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	2 (4.4)	4 (5.3)
Number of Subjects Censored, n (%)	43 (95.6)	72 (94.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.764 (0.959)
95% CI		(0.117, 5.002)
Log-rank p-value		0.705

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (89.5, 100.0)	95.9 (91.3, 100.0)
6 months	NE (NE, NE)	91.7 (82.6, 100.0)
9 months	NE (NE, NE)	91.7 (82.6, 100.0)
12 months	NE (NE, NE)	91.7 (82.6, 100.0)
18 months	NE (NE, NE)	91.7 (82.6, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	5 (6.6)
Number of Subjects Censored, n (%)	45 (100.0)	71 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.124

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	92.8 (86.7, 98.9)
6 months	NE (NE, NE)	92.8 (86.7, 98.9)
9 months	NE (NE, NE)	92.8 (86.7, 98.9)
12 months	NE (NE, NE)	92.8 (86.7, 98.9)
18 months	NE (NE, NE)	92.8 (86.7, 98.9)
Median Follow-up Time (months)	2.83	3.40

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	1 (2.2)	2 (2.6)
Number of Subjects Censored, n (%)	44 (97.8)	74 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.382 (1.336)
95% CI		(0.101, 18.975)
Log-rank p-value		0.719

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (92.3, 100.0)	96.7 (92.2, 100.0)
6 months	NE (NE, NE)	96.7 (92.2, 100.0)
9 months	NE (NE, NE)	96.7 (92.2, 100.0)
12 months	NE (NE, NE)	96.7 (92.2, 100.0)
18 months	NE (NE, NE)	96.7 (92.2, 100.0)
Median Follow-up Time (months)	2.83	3.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	1 (1.3)
Number of Subjects Censored, n (%)	45 (100.0)	75 (98.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.533

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.0 (94.1, 100.0)
6 months	NE (NE, NE)	98.0 (94.1, 100.0)
9 months	NE (NE, NE)	98.0 (94.1, 100.0)
12 months	NE (NE, NE)	98.0 (94.1, 100.0)
18 months	NE (NE, NE)	98.0 (94.1, 100.0)
Median Follow-up Time (months)	2.83	3.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	1 (1.3)
Number of Subjects Censored, n (%)	45 (100.0)	75 (98.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.508

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.5 (95.5, 100.0)
6 months	NE (NE, NE)	98.5 (95.5, 100.0)
9 months	NE (NE, NE)	98.5 (95.5, 100.0)
12 months	NE (NE, NE)	98.5 (95.5, 100.0)
18 months	NE (NE, NE)	98.5 (95.5, 100.0)
Median Follow-up Time (months)	2.83	3.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	9 (20.0)	19 (25.0)
Number of Subjects Censored, n (%)	36 (80.0)	57 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.82, NE)	4.80 (1.05, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.332 (0.411)
95% CI		(0.595, 2.980)
Log-rank p-value		0.489

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.3 (65.5, 91.1)	75.5 (65.7, 85.4)
6 months	NE (NE, NE)	72.1 (60.6, 83.6)
9 months	NE (NE, NE)	72.1 (60.6, 83.6)
12 months	NE (NE, NE)	72.1 (60.6, 83.6)
18 months	NE (NE, NE)	72.1 (60.6, 83.6)
Median Follow-up Time (months)	2.83	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	3 (6.7)	12 (15.8)
Number of Subjects Censored, n (%)	42 (93.3)	64 (84.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.61, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.746 (0.653)
95% CI		(0.763, 9.882)
Log-rank p-value		0.110

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.5 (84.1, 100.0)	83.8 (75.4, 92.2)
6 months	NE (NE, NE)	83.8 (75.4, 92.2)
9 months	NE (NE, NE)	83.8 (75.4, 92.2)
12 months	NE (NE, NE)	83.8 (75.4, 92.2)
18 months	NE (NE, NE)	83.8 (75.4, 92.2)
Median Follow-up Time (months)	2.83	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	2 (4.4)	2 (2.6)
Number of Subjects Censored, n (%)	43 (95.6)	74 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 5.6*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.692 (1.006)
95% CI		(0.096, 4.971)
Log-rank p-value		0.729

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (89.5, 100.0)	97.3 (93.5, 100.0)
6 months	NE (NE, NE)	97.3 (93.5, 100.0)
9 months	NE (NE, NE)	97.3 (93.5, 100.0)
12 months	NE (NE, NE)	97.3 (93.5, 100.0)
18 months	NE (NE, NE)	97.3 (93.5, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	3 (6.7)	2 (2.6)
Number of Subjects Censored, n (%)	42 (93.3)	74 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.375 (0.932)
95% CI		(0.060, 2.331)
Log-rank p-value		0.257

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.2 (85.8, 100.0)	97.4 (93.7, 100.0)
6 months	NE (NE, NE)	97.4 (93.7, 100.0)
9 months	NE (NE, NE)	97.4 (93.7, 100.0)
12 months	NE (NE, NE)	97.4 (93.7, 100.0)
18 months	NE (NE, NE)	97.4 (93.7, 100.0)
Median Follow-up Time (months)	2.83	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	2 (2.6)
Number of Subjects Censored, n (%)	45 (100.0)	74 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.453

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.1 (93.2, 100.0)
6 months	NE (NE, NE)	97.1 (93.2, 100.0)
9 months	NE (NE, NE)	97.1 (93.2, 100.0)
12 months	NE (NE, NE)	97.1 (93.2, 100.0)
18 months	NE (NE, NE)	97.1 (93.2, 100.0)
Median Follow-up Time (months)	2.83	3.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	1 (1.3)
Number of Subjects Censored, n (%)	45 (100.0)	75 (98.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	96.3 (89.2, 100.0)
9 months	NE (NE, NE)	96.3 (89.2, 100.0)
12 months	NE (NE, NE)	96.3 (89.2, 100.0)
18 months	NE (NE, NE)	96.3 (89.2, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Vascular disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	3 (6.7)	25 (32.9)
Number of Subjects Censored, n (%)	42 (93.3)	51 (67.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.05 (0.69, 6.93)
Median (95% CI)	NE (NE, NE)	NE (6.93, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 5.6*	0.1, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.312 (0.621)
95% CI		(1.571, 17.957)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Vascular disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.4 (83.9, 100.0)	68.2 (57.2, 79.1)
6 months	NE (NE, NE)	65.2 (53.2, 77.1)
9 months	NE (NE, NE)	57.0 (38.8, 75.3)
12 months	NE (NE, NE)	57.0 (38.8, 75.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	2 (4.4)	25 (32.9)
Number of Subjects Censored, n (%)	43 (95.6)	51 (67.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.61 (0.69, 6.93)
Median (95% CI)	NE (NE, NE)	NE (6.93, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 5.6*	0.1, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		7.425 (0.744)
95% CI		(1.729, 31.894)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.6 (87.3, 100.0)	69.5 (58.7, 80.4)
6 months	NE (NE, NE)	66.6 (54.8, 78.4)
9 months	NE (NE, NE)	51.8 (31.5, 72.1)
12 months	NE (NE, NE)	51.8 (31.5, 72.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	9 (20.0)	18 (23.7)
Number of Subjects Censored, n (%)	36 (80.0)	58 (76.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.25, NE)	5.16 (1.61, NE)
Median (95% CI)	NE (NE, NE)	NE (7.66, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.890 (0.440)
95% CI		(0.375, 2.108)
Log-rank p-value		0.881

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.4 (65.7, 91.1)	80.6 (71.3, 89.8)
6 months	NE (NE, NE)	69.0 (54.4, 83.5)
9 months	NE (NE, NE)	62.1 (43.7, 80.4)
12 months	NE (NE, NE)	62.1 (43.7, 80.4)
18 months	NE (NE, NE)	62.1 (43.7, 80.4)
Median Follow-up Time (months)	2.79	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	1 (2.2)	7 (9.2)
Number of Subjects Censored, n (%)	44 (97.8)	69 (90.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.70, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.019 (1.099)
95% CI		(0.466, 34.676)
Log-rank p-value		0.147

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (92.8, 100.0)	91.1 (84.2, 98.0)
6 months	NE (NE, NE)	87.5 (77.8, 97.1)
9 months	NE (NE, NE)	87.5 (77.8, 97.1)
12 months	NE (NE, NE)	87.5 (77.8, 97.1)
18 months	NE (NE, NE)	87.5 (77.8, 97.1)
Median Follow-up Time (months)	2.83	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	4 (8.9)	4 (5.3)
Number of Subjects Censored, n (%)	41 (91.1)	72 (94.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.569 (0.718)
95% CI		(0.139, 2.324)
Log-rank p-value		0.416

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.8 (82.3, 99.4)	94.7 (89.7, 99.8)
6 months	NE (NE, NE)	94.7 (89.7, 99.8)
9 months	NE (NE, NE)	94.7 (89.7, 99.8)
12 months	NE (NE, NE)	94.7 (89.7, 99.8)
18 months	NE (NE, NE)	94.7 (89.7, 99.8)
Median Follow-up Time (months)	2.83	3.47

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	2 (4.4)	2 (2.6)
Number of Subjects Censored, n (%)	43 (95.6)	74 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.509 (1.101)
95% CI		(0.059, 4.399)
Log-rank p-value		0.624

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.3 (88.9, 100.0)	98.7 (96.1, 100.0)
6 months	NE (NE, NE)	94.6 (86.3, 100.0)
9 months	NE (NE, NE)	94.6 (86.3, 100.0)
12 months	NE (NE, NE)	94.6 (86.3, 100.0)
18 months	NE (NE, NE)	94.6 (86.3, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	1 (1.3)
Number of Subjects Censored, n (%)	45 (100.0)	75 (98.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.70, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	94.1 (82.9, 100.0)
12 months	NE (NE, NE)	94.1 (82.9, 100.0)
18 months	NE (NE, NE)	94.1 (82.9, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	1 (1.3)
Number of Subjects Censored, n (%)	45 (100.0)	75 (98.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.527

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.7 (96.1, 100.0)
6 months	NE (NE, NE)	98.7 (96.1, 100.0)
9 months	NE (NE, NE)	98.7 (96.1, 100.0)
12 months	NE (NE, NE)	98.7 (96.1, 100.0)
18 months	NE (NE, NE)	98.7 (96.1, 100.0)
Median Follow-up Time (months)	2.83	3.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	3 (6.7)	21 (27.6)
Number of Subjects Censored, n (%)	42 (93.3)	55 (72.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.45 (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.344 (0.627)
95% CI		(1.270, 14.857)
Log-rank p-value		0.011

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.2 (85.7, 100.0)	73.4 (63.4, 83.4)
6 months	NE (NE, NE)	69.1 (56.6, 81.6)
9 months	NE (NE, NE)	69.1 (56.6, 81.6)
12 months	NE (NE, NE)	69.1 (56.6, 81.6)
18 months	NE (NE, NE)	69.1 (56.6, 81.6)
Median Follow-up Time (months)	2.83	2.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	9 (11.8)
Number of Subjects Censored, n (%)	45 (100.0)	67 (88.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.19, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.028

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	89.1 (82.0, 96.3)
6 months	NE (NE, NE)	84.7 (73.8, 95.6)
9 months	NE (NE, NE)	84.7 (73.8, 95.6)
12 months	NE (NE, NE)	84.7 (73.8, 95.6)
18 months	NE (NE, NE)	84.7 (73.8, 95.6)
Median Follow-up Time (months)	2.83	3.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	3 (3.9)
Number of Subjects Censored, n (%)	45 (100.0)	73 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.174

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.1 (91.7, 100.0)
6 months	NE (NE, NE)	96.1 (91.7, 100.0)
9 months	NE (NE, NE)	96.1 (91.7, 100.0)
12 months	NE (NE, NE)	96.1 (91.7, 100.0)
18 months	NE (NE, NE)	96.1 (91.7, 100.0)
Median Follow-up Time (months)	2.83	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	3 (3.9)
Number of Subjects Censored, n (%)	45 (100.0)	73 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.062

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.0 (91.6, 100.0)
6 months	NE (NE, NE)	96.0 (91.6, 100.0)
9 months	NE (NE, NE)	96.0 (91.6, 100.0)
12 months	NE (NE, NE)	96.0 (91.6, 100.0)
18 months	NE (NE, NE)	96.0 (91.6, 100.0)
Median Follow-up Time (months)	2.83	3.47

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Nervous system disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	7 (15.6)	19 (25.0)
Number of Subjects Censored, n (%)	38 (84.4)	57 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.92, NE)	3.98 (0.76, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.601 (0.454)
95% CI		(0.657, 3.900)
Log-rank p-value		0.297

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Nervous system disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.3 (73.5, 95.0)	78.7 (69.4, 88.0)
6 months	NE (NE, NE)	70.1 (57.5, 82.6)
9 months	NE (NE, NE)	70.1 (57.5, 82.6)
12 months	NE (NE, NE)	70.1 (57.5, 82.6)
18 months	NE (NE, NE)	70.1 (57.5, 82.6)
Median Follow-up Time (months)	2.83	3.14

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	2 (4.4)	6 (7.9)
Number of Subjects Censored, n (%)	43 (95.6)	70 (92.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.231 (0.822)
95% CI		(0.446, 11.169)
Log-rank p-value		0.310

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (89.2, 100.0)	91.9 (85.7, 98.1)
6 months	NE (NE, NE)	91.9 (85.7, 98.1)
9 months	NE (NE, NE)	91.9 (85.7, 98.1)
12 months	NE (NE, NE)	91.9 (85.7, 98.1)
18 months	NE (NE, NE)	91.9 (85.7, 98.1)
Median Follow-up Time (months)	2.83	3.33

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	2 (4.4)	3 (3.9)
Number of Subjects Censored, n (%)	43 (95.6)	73 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.539 (1.019)
95% CI		(0.073, 3.973)
Log-rank p-value		0.501

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (89.5, 100.0)	96.0 (91.6, 100.0)
6 months	NE (NE, NE)	96.0 (91.6, 100.0)
9 months	NE (NE, NE)	96.0 (91.6, 100.0)
12 months	NE (NE, NE)	96.0 (91.6, 100.0)
18 months	NE (NE, NE)	96.0 (91.6, 100.0)
Median Follow-up Time (months)	2.83	3.47

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	2 (2.6)
Number of Subjects Censored, n (%)	45 (100.0)	74 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.276

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.4 (93.8, 100.0)
6 months	NE (NE, NE)	97.4 (93.8, 100.0)
9 months	NE (NE, NE)	97.4 (93.8, 100.0)
12 months	NE (NE, NE)	97.4 (93.8, 100.0)
18 months	NE (NE, NE)	97.4 (93.8, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	4 (8.9)	10 (13.2)
Number of Subjects Censored, n (%)	41 (91.1)	66 (86.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.93, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 5.6*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.934 (0.650)
95% CI		(0.261, 3.336)
Log-rank p-value		0.994

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.9 (82.3, 99.4)	87.3 (79.5, 95.1)
6 months	NE (NE, NE)	87.3 (79.5, 95.1)
9 months	NE (NE, NE)	80.0 (64.6, 95.5)
12 months	NE (NE, NE)	80.0 (64.6, 95.5)
18 months	NE (NE, NE)	80.0 (64.6, 95.5)
Median Follow-up Time (months)	2.83	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	1 (2.2)	9 (11.8)
Number of Subjects Censored, n (%)	44 (97.8)	67 (88.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.93, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.117 (1.084)
95% CI		(0.492, 34.440)
Log-rank p-value		0.146

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (93.5, 100.0)	88.6 (81.2, 96.1)
6 months	NE (NE, NE)	88.6 (81.2, 96.1)
9 months	NE (NE, NE)	81.8 (67.3, 96.4)
12 months	NE (NE, NE)	81.8 (67.3, 96.4)
18 months	NE (NE, NE)	81.8 (67.3, 96.4)
Median Follow-up Time (months)	2.83	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	2 (4.4)	1 (1.3)
Number of Subjects Censored, n (%)	43 (95.6)	75 (98.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.090 (1.447)
95% CI		(0.005, 1.541)
Log-rank p-value		0.068

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.3 (89.0, 100.0)	98.7 (96.1, 100.0)
6 months	NE (NE, NE)	98.7 (96.1, 100.0)
9 months	NE (NE, NE)	98.7 (96.1, 100.0)
12 months	NE (NE, NE)	98.7 (96.1, 100.0)
18 months	NE (NE, NE)	98.7 (96.1, 100.0)
Median Follow-up Time (months)	2.83	3.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Infections and infestations**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	5 (11.1)	15 (19.7)
Number of Subjects Censored, n (%)	40 (88.9)	61 (80.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	6.87 (3.32, NE)
Median (95% CI)	NE (NE, NE)	17.48 (17.48, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.48, NE)
Min, Max	0.0, 5.6*	0.2, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.022 (0.551)
95% CI		(0.347, 3.006)
Log-rank p-value		0.909

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Infections and infestations**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.0 (82.6, 99.4)	87.7 (80.2, 95.3)
6 months	NE (NE, NE)	75.8 (62.7, 89.0)
9 months	NE (NE, NE)	70.0 (53.6, 86.4)
12 months	NE (NE, NE)	70.0 (53.6, 86.4)
18 months	NE (NE, NE)	35.0 (0.0, 84.2)
Median Follow-up Time (months)	2.83	3.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	3 (6.7)	3 (3.9)
Number of Subjects Censored, n (%)	42 (93.3)	73 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (3.71, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.315 (0.969)
95% CI		(0.047, 2.102)
Log-rank p-value		0.300

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (89.5, 100.0)	97.4 (93.7, 100.0)
6 months	NE (NE, NE)	93.1 (84.3, 100.0)
9 months	NE (NE, NE)	93.1 (84.3, 100.0)
12 months	NE (NE, NE)	93.1 (84.3, 100.0)
18 months	NE (NE, NE)	93.1 (84.3, 100.0)
Median Follow-up Time (months)	2.83	3.47

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	1 (2.2)	0
Number of Subjects Censored, n (%)	44 (97.8)	76 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.114

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (93.3, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	6 (13.3)	13 (17.1)
Number of Subjects Censored, n (%)	39 (86.7)	63 (82.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.68, NE)	NE (2.27, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 5.6*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.281 (0.503)
95% CI		(0.478, 3.433)
Log-rank p-value		0.615

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.6 (76.6, 96.6)	83.2 (74.4, 92.0)
6 months	NE (NE, NE)	81.1 (71.6, 90.6)
9 months	NE (NE, NE)	81.1 (71.6, 90.6)
12 months	NE (NE, NE)	81.1 (71.6, 90.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	3 (6.7)	7 (9.2)
Number of Subjects Censored, n (%)	42 (93.3)	69 (90.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	17.74 (17.74, NE)
Median (95% CI)	NE (NE, NE)	17.74 (17.74, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.74, NE)
Min, Max	0.7, 5.6*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.257 (0.718)
95% CI		(0.308, 5.135)
Log-rank p-value		0.764

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.3 (86.0, 100.0)	93.1 (87.2, 98.9)
6 months	NE (NE, NE)	91.1 (84.2, 98.0)
9 months	NE (NE, NE)	91.1 (84.2, 98.0)
12 months	NE (NE, NE)	91.1 (84.2, 98.0)
18 months	NE (NE, NE)	45.5 (0.0, 100.0)
Median Follow-up Time (months)	2.83	3.40

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	1 (2.2)	9 (11.8)
Number of Subjects Censored, n (%)	44 (97.8)	67 (88.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.7, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.460 (1.061)
95% CI		(0.683, 43.643)
Log-rank p-value		0.071

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (93.5, 100.0)	87.4 (79.5, 95.2)
6 months	NE (NE, NE)	87.4 (79.5, 95.2)
9 months	NE (NE, NE)	87.4 (79.5, 95.2)
12 months	NE (NE, NE)	87.4 (79.5, 95.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Endocrine disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	19 (25.0)
Number of Subjects Censored, n (%)	45 (100.0)	57 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.81 (1.87, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.7, 12.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Endocrine disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	79.0 (69.5, 88.5)
6 months	NE (NE, NE)	66.8 (53.2, 80.5)
9 months	NE (NE, NE)	66.8 (53.2, 80.5)
12 months	NE (NE, NE)	66.8 (53.2, 80.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	19 (25.0)
Number of Subjects Censored, n (%)	45 (100.0)	57 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.81 (1.87, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.7, 12.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	79.0 (69.5, 88.5)
6 months	NE (NE, NE)	66.8 (53.2, 80.5)
9 months	NE (NE, NE)	66.8 (53.2, 80.5)
12 months	NE (NE, NE)	66.8 (53.2, 80.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Psychiatric disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	5 (11.1)	9 (11.8)
Number of Subjects Censored, n (%)	40 (88.9)	67 (88.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.14, NE)	NE (3.98, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.058 (0.588)
95% CI		(0.334, 3.354)
Log-rank p-value		0.978

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Psychiatric disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.7 (77.5, 97.9)	88.9 (81.6, 96.2)
6 months	NE (NE, NE)	86.0 (77.0, 95.0)
9 months	NE (NE, NE)	86.0 (77.0, 95.0)
12 months	NE (NE, NE)	86.0 (77.0, 95.0)
18 months	NE (NE, NE)	86.0 (77.0, 95.0)
Median Follow-up Time (months)	2.83	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	4 (8.9)	2 (2.6)
Number of Subjects Censored, n (%)	41 (91.1)	74 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.183 (0.971)
95% CI		(0.027, 1.229)
Log-rank p-value		0.043

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.4 (81.3, 99.4)	97.0 (92.9, 100.0)
6 months	NE (NE, NE)	97.0 (92.9, 100.0)
9 months	NE (NE, NE)	97.0 (92.9, 100.0)
12 months	NE (NE, NE)	97.0 (92.9, 100.0)
18 months	NE (NE, NE)	97.0 (92.9, 100.0)
Median Follow-up Time (months)	2.83	3.47

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	3 (3.9)
Number of Subjects Censored, n (%)	45 (100.0)	73 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.183

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.8 (91.1, 100.0)
6 months	NE (NE, NE)	95.8 (91.1, 100.0)
9 months	NE (NE, NE)	95.8 (91.1, 100.0)
12 months	NE (NE, NE)	95.8 (91.1, 100.0)
18 months	NE (NE, NE)	95.8 (91.1, 100.0)
Median Follow-up Time (months)	2.83	3.47

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	1 (2.2)	4 (5.3)
Number of Subjects Censored, n (%)	44 (97.8)	72 (94.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.882 (1.146)
95% CI		(0.411, 36.689)
Log-rank p-value		0.188

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (92.3, 100.0)	94.6 (89.4, 99.8)
6 months	NE (NE, NE)	94.6 (89.4, 99.8)
9 months	NE (NE, NE)	94.6 (89.4, 99.8)
12 months	NE (NE, NE)	94.6 (89.4, 99.8)
18 months	NE (NE, NE)	94.6 (89.4, 99.8)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	1 (2.2)	3 (3.9)
Number of Subjects Censored, n (%)	44 (97.8)	73 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.62, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.586 (1.427)
95% CI		(0.036, 9.601)
Log-rank p-value		0.898

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (93.5, 100.0)	98.7 (96.1, 100.0)
6 months	NE (NE, NE)	98.7 (96.1, 100.0)
9 months	NE (NE, NE)	92.1 (79.4, 100.0)
12 months	NE (NE, NE)	83.7 (64.3, 100.0)
18 months	NE (NE, NE)	83.7 (64.3, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	1 (1.3)
Number of Subjects Censored, n (%)	45 (100.0)	75 (98.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.66, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	90.9 (73.9, 100.0)
18 months	NE (NE, NE)	90.9 (73.9, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Number of Subjects with Events, n (%)	0	1 (1.3)
Number of Subjects Censored, n (%)	45 (100.0)	75 (98.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.62, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
<=3

Statistics	Placebo + BSC N=45	Fruquintinib + BSC N=76
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	93.3 (80.7, 100.0)
12 months	NE (NE, NE)	93.3 (80.7, 100.0)
18 months	NE (NE, NE)	93.3 (80.7, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	110 (59.5)	274 (72.1)
Number of Subjects Censored, n (%)	75 (40.5)	106 (27.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.46, 0.69)	0.36 (0.26, 0.49)
Median (95% CI)	1.61 (1.15, 2.56)	0.99 (0.72, 1.51)
75% percentile (95% CI)	NE (4.70, NE)	5.55 (3.91, 7.29)
Min, Max	0.0, 13.0*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.220 (0.114)
95% CI		(0.976, 1.525)
Log-rank p-value		0.084

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	40.4 (33.0, 47.8)	35.4 (30.5, 40.3)
6 months	30.3 (19.2, 41.4)	22.6 (17.5, 27.7)
9 months	30.3 (19.2, 41.4)	16.5 (10.5, 22.5)
12 months	30.3 (19.2, 41.4)	16.5 (10.5, 22.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.41	0.97

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	44 (23.8)	137 (36.1)
Number of Subjects Censored, n (%)	141 (76.2)	243 (63.9)
Time to first TEAE (months)		
25% percentile (95% CI)	3.22 (0.95, NE)	0.99 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.431 (0.174)
95% CI		(1.016, 2.014)
Log-rank p-value		0.037

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.7 (69.2, 82.2)	66.2 (61.4, 71.1)
6 months	68.5 (56.7, 80.2)	61.6 (56.3, 66.9)
9 months	68.5 (56.7, 80.2)	58.4 (51.4, 65.3)
12 months	68.5 (56.7, 80.2)	58.4 (51.4, 65.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.37	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	30 (16.2)	79 (20.8)
Number of Subjects Censored, n (%)	155 (83.8)	301 (79.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	7.29 (3.68, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.153 (0.216)
95% CI		(0.755, 1.762)
Log-rank p-value		0.556

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.4 (76.6, 88.2)	80.7 (76.6, 84.7)
6 months	82.4 (76.6, 88.2)	77.6 (72.9, 82.2)
9 months	82.4 (76.6, 88.2)	75.0 (69.3, 80.7)
12 months	82.4 (76.6, 88.2)	75.0 (69.3, 80.7)
18 months	NE (NE, NE)	75.0 (69.3, 80.7)
Median Follow-up Time (months)	2.56	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	19 (10.3)	42 (11.1)
Number of Subjects Censored, n (%)	166 (89.7)	338 (88.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.70, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.885 (0.283)
95% CI		(0.509, 1.540)
Log-rank p-value		0.588

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.3 (84.6, 94.1)	91.0 (88.1, 93.9)
6 months	84.1 (73.1, 95.0)	87.9 (84.1, 91.7)
9 months	84.1 (73.1, 95.0)	86.2 (81.8, 90.6)
12 months	84.1 (73.1, 95.0)	79.5 (66.4, 92.7)
18 months	NE (NE, NE)	79.5 (66.4, 92.7)
Median Follow-up Time (months)	2.76	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	5 (2.7)	52 (13.7)
Number of Subjects Censored, n (%)	180 (97.3)	328 (86.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
Median (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.24, NE)
Min, Max	0.1, 13.0*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.618 (0.470)
95% CI		(1.839, 11.595)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.0 (94.4, 99.6)	87.3 (83.9, 90.7)
6 months	97.0 (94.4, 99.6)	85.8 (82.1, 89.6)
9 months	97.0 (94.4, 99.6)	84.7 (80.3, 89.0)
12 months	97.0 (94.4, 99.6)	84.7 (80.3, 89.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	25 (13.5)	22 (5.8)
Number of Subjects Censored, n (%)	160 (86.5)	358 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.288 (0.301)
95% CI		(0.160, 0.520)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.9 (80.4, 91.3)	96.6 (94.7, 98.5)
6 months	81.5 (73.7, 89.4)	91.8 (88.2, 95.4)
9 months	81.5 (73.7, 89.4)	91.8 (88.2, 95.4)
12 months	81.5 (73.7, 89.4)	91.8 (88.2, 95.4)
18 months	NE (NE, NE)	82.7 (65.3, 100.0)
Median Follow-up Time (months)	2.79	4.01

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	15 (8.1)	20 (5.3)
Number of Subjects Censored, n (%)	170 (91.9)	360 (94.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.535 (0.349)
95% CI		(0.270, 1.060)
Log-rank p-value		0.066

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.6 (87.6, 95.7)	95.0 (92.8, 97.3)
6 months	91.6 (87.6, 95.7)	95.0 (92.8, 97.3)
9 months	91.6 (87.6, 95.7)	92.4 (86.8, 97.9)
12 months	91.6 (87.6, 95.7)	88.5 (79.4, 97.6)
18 months	NE (NE, NE)	88.5 (79.4, 97.6)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	4 (2.2)	13 (3.4)
Number of Subjects Censored, n (%)	181 (97.8)	367 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.106 (0.587)
95% CI		(0.350, 3.495)
Log-rank p-value		0.944

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.7, 99.9)	97.8 (96.3, 99.3)
6 months	97.8 (95.7, 99.9)	95.8 (93.3, 98.3)
9 months	97.8 (95.7, 99.9)	95.8 (93.3, 98.3)
12 months	97.8 (95.7, 99.9)	92.1 (84.6, 99.6)
18 months	NE (NE, NE)	92.1 (84.6, 99.6)
Median Follow-up Time (months)	2.83	4.01

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	4 (2.2)	10 (2.6)
Number of Subjects Censored, n (%)	181 (97.8)	370 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.891 (0.600)
95% CI		(0.275, 2.886)
Log-rank p-value		0.844

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (94.3, 100.0)	97.7 (96.0, 99.3)
6 months	97.2 (94.3, 100.0)	96.6 (94.4, 98.8)
9 months	97.2 (94.3, 100.0)	96.6 (94.4, 98.8)
12 months	97.2 (94.3, 100.0)	96.6 (94.4, 98.8)
18 months	NE (NE, NE)	96.6 (94.4, 98.8)
Median Follow-up Time (months)	2.83	3.96

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	2 (1.1)	9 (2.4)
Number of Subjects Censored, n (%)	183 (98.9)	371 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.740 (0.793)
95% CI		(0.368, 8.239)
Log-rank p-value		0.474

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (97.4, 100.0)	98.1 (96.8, 99.5)
6 months	98.9 (97.4, 100.0)	96.8 (94.4, 99.1)
9 months	98.9 (97.4, 100.0)	96.8 (94.4, 99.1)
12 months	98.9 (97.4, 100.0)	96.8 (94.4, 99.1)
18 months	NE (NE, NE)	96.8 (94.4, 99.1)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	105 (56.8)	262 (68.9)
Number of Subjects Censored, n (%)	80 (43.2)	118 (31.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.62 (0.39, 0.69)	0.46 (0.39, 0.62)
Median (95% CI)	1.71 (1.31, 2.92)	1.38 (0.95, 1.84)
75% percentile (95% CI)	5.36 (3.75, NE)	5.55 (4.50, NE)
Min, Max	0.0, 6.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.090 (0.117)
95% CI		(0.866, 1.371)
Log-rank p-value		0.445

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	40.5 (32.3, 48.8)	36.8 (31.8, 41.8)
6 months	9.7 (0.0, 25.8)	24.0 (18.5, 29.5)
9 months	NE (NE, NE)	20.6 (14.7, 26.6)
12 months	NE (NE, NE)	17.2 (9.3, 25.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.38	1.28

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	18 (9.7)	99 (26.1)
Number of Subjects Censored, n (%)	167 (90.3)	281 (73.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.71 (2.10, 6.47)
Median (95% CI)	NE (NE, NE)	NE (10.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.359 (0.258)
95% CI		(1.422, 3.913)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.8 (85.4, 94.3)	77.1 (72.8, 81.4)
6 months	89.8 (85.4, 94.3)	70.0 (64.3, 75.7)
9 months	89.8 (85.4, 94.3)	66.5 (59.8, 73.2)
12 months	89.8 (85.4, 94.3)	59.1 (44.2, 74.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	2.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	32 (17.3)	73 (19.2)
Number of Subjects Censored, n (%)	153 (82.7)	307 (80.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	6.44 (4.63, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.841 (0.216)
95% CI		(0.550, 1.285)
Log-rank p-value		0.441

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.2 (76.4, 88.0)	83.3 (79.3, 87.2)
6 months	77.9 (68.0, 87.8)	76.7 (71.5, 82.0)
9 months	77.9 (68.0, 87.8)	73.2 (66.7, 79.7)
12 months	77.9 (68.0, 87.8)	73.2 (66.7, 79.7)
18 months	NE (NE, NE)	73.2 (66.7, 79.7)
Median Follow-up Time (months)	2.56	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	30 (16.2)	69 (18.2)
Number of Subjects Censored, n (%)	155 (83.8)	311 (81.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.92, NE)	10.12 (5.19, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.855 (0.223)
95% CI		(0.553, 1.323)
Log-rank p-value		0.587

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.8 (75.3, 88.3)	84.3 (80.5, 88.2)
6 months	77.9 (68.2, 87.6)	79.0 (74.1, 83.9)
9 months	77.9 (68.2, 87.6)	75.7 (69.7, 81.7)
12 months	77.9 (68.2, 87.6)	72.0 (62.7, 81.2)
18 months	NE (NE, NE)	72.0 (62.7, 81.2)
Median Follow-up Time (months)	2.63	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	18 (9.7)	70 (18.4)
Number of Subjects Censored, n (%)	167 (90.3)	310 (81.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	9.33 (4.21, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.454 (0.268)
95% CI		(0.860, 2.459)
Log-rank p-value		0.162

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.6 (82.9, 94.4)	84.1 (80.2, 88.0)
6 months	86.5 (79.6, 93.5)	79.0 (74.2, 83.8)
9 months	86.5 (79.6, 93.5)	75.3 (69.2, 81.5)
12 months	86.5 (79.6, 93.5)	72.3 (64.1, 80.6)
18 months	NE (NE, NE)	72.3 (64.1, 80.6)
Median Follow-up Time (months)	2.69	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	21 (11.4)	60 (15.8)
Number of Subjects Censored, n (%)	164 (88.6)	320 (84.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.36, NE)	18.04 (6.47, NE)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.1, 13.0*	0.0, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.048 (0.259)
95% CI		(0.631, 1.741)
Log-rank p-value		0.819

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.6 (83.7, 93.5)	87.5 (84.1, 90.9)
6 months	80.8 (68.8, 92.8)	81.7 (77.0, 86.5)
9 months	80.8 (68.8, 92.8)	78.7 (72.9, 84.5)
12 months	80.8 (68.8, 92.8)	75.3 (66.7, 83.8)
18 months	NE (NE, NE)	75.3 (66.7, 83.8)
Median Follow-up Time (months)	2.79	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	7 (3.8)	59 (15.5)
Number of Subjects Censored, n (%)	178 (96.2)	321 (84.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.096 (0.401)
95% CI		(1.865, 8.996)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.8 (92.8, 98.9)	85.7 (82.2, 89.3)
6 months	95.8 (92.8, 98.9)	83.1 (78.9, 87.2)
9 months	95.8 (92.8, 98.9)	81.6 (76.5, 86.6)
12 months	95.8 (92.8, 98.9)	81.6 (76.5, 86.6)
18 months	NE (NE, NE)	81.6 (76.5, 86.6)
Median Follow-up Time (months)	2.79	3.52

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	6 (3.2)	26 (6.8)
Number of Subjects Censored, n (%)	179 (96.8)	354 (93.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.581 (0.459)
95% CI		(0.642, 3.890)
Log-rank p-value		0.345

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (94.5, 99.6)	94.5 (92.2, 96.9)
6 months	90.1 (76.8, 100.0)	91.3 (87.8, 94.7)
9 months	NE (NE, NE)	91.3 (87.8, 94.7)
12 months	NE (NE, NE)	91.3 (87.8, 94.7)
18 months	NE (NE, NE)	91.3 (87.8, 94.7)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	3 (1.6)	15 (3.9)
Number of Subjects Censored, n (%)	182 (98.4)	365 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.002 (0.642)
95% CI		(0.569, 7.044)
Log-rank p-value		0.274

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (96.2, 100.0)	96.8 (95.0, 98.6)
6 months	98.2 (96.2, 100.0)	95.5 (92.9, 98.0)
9 months	98.2 (96.2, 100.0)	94.0 (90.1, 97.8)
12 months	98.2 (96.2, 100.0)	94.0 (90.1, 97.8)
18 months	NE (NE, NE)	94.0 (90.1, 97.8)
Median Follow-up Time (months)	2.79	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	3 (1.6)	10 (2.6)
Number of Subjects Censored, n (%)	182 (98.4)	370 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.534 (0.661)
95% CI		(0.420, 5.597)
Log-rank p-value		0.468

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (96.3, 100.0)	97.2 (95.5, 98.9)
6 months	98.3 (96.3, 100.0)	97.2 (95.5, 98.9)
9 months	98.3 (96.3, 100.0)	97.2 (95.5, 98.9)
12 months	98.3 (96.3, 100.0)	97.2 (95.5, 98.9)
18 months	NE (NE, NE)	97.2 (95.5, 98.9)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	9 (4.9)	3 (0.8)
Number of Subjects Censored, n (%)	176 (95.1)	377 (99.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.119 (0.687)
95% CI		(0.031, 0.457)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.6 (91.2, 98.1)	99.4 (98.7, 100.0)
6 months	94.6 (91.2, 98.1)	98.6 (96.8, 100.0)
9 months	94.6 (91.2, 98.1)	98.6 (96.8, 100.0)
12 months	94.6 (91.2, 98.1)	98.6 (96.8, 100.0)
18 months	NE (NE, NE)	98.6 (96.8, 100.0)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	0	13 (3.4)
Number of Subjects Censored, n (%)	185 (100.0)	367 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.019

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.6 (94.7, 98.5)
6 months	100.0 (100.0, 100.0)	96.6 (94.7, 98.5)
9 months	100.0 (100.0, 100.0)	94.9 (91.2, 98.7)
12 months	100.0 (100.0, 100.0)	94.9 (91.2, 98.7)
18 months	NE (NE, NE)	94.9 (91.2, 98.7)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	53 (28.6)	169 (44.5)
Number of Subjects Censored, n (%)	132 (71.4)	211 (55.5)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.89, 4.27)	1.15 (0.92, 1.61)
Median (95% CI)	10.18 (NE, NE)	6.24 (4.60, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.0, 10.2	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.383 (0.159)
95% CI		(1.013, 1.887)
Log-rank p-value		0.052

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.2 (64.4, 78.1)	58.4 (53.2, 63.5)
6 months	65.2 (54.7, 75.6)	52.1 (46.4, 57.9)
9 months	65.2 (54.7, 75.6)	48.2 (41.9, 54.4)
12 months	0.0 (NE, NE)	45.0 (36.5, 53.4)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.33	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	34 (18.4)	114 (30.0)
Number of Subjects Censored, n (%)	151 (81.6)	266 (70.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.91, NE)	2.56 (1.61, 3.52)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.448 (0.197)
95% CI		(0.984, 2.131)
Log-rank p-value		0.074

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.0 (75.2, 86.9)	71.5 (66.8, 76.3)
6 months	77.3 (68.3, 86.4)	67.5 (62.3, 72.8)
9 months	77.3 (68.3, 86.4)	64.8 (58.8, 70.7)
12 months	77.3 (68.3, 86.4)	62.0 (54.1, 69.8)
18 months	NE (NE, NE)	62.0 (54.1, 69.8)
Median Follow-up Time (months)	2.56	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	4 (2.2)	25 (6.6)
Number of Subjects Censored, n (%)	181 (97.8)	355 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.510 (0.541)
95% CI		(0.870, 7.245)
Log-rank p-value		0.065

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.7, 99.9)	93.3 (90.7, 96.0)
6 months	97.8 (95.7, 99.9)	92.4 (89.4, 95.3)
9 months	97.8 (95.7, 99.9)	92.4 (89.4, 95.3)
12 months	97.8 (95.7, 99.9)	92.4 (89.4, 95.3)
18 months	NE (NE, NE)	92.4 (89.4, 95.3)
Median Follow-up Time (months)	2.79	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	5 (2.7)	17 (4.5)
Number of Subjects Censored, n (%)	180 (97.3)	363 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.120 (0.522)
95% CI		(0.402, 3.117)
Log-rank p-value		0.746

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.6, 99.9)	96.6 (94.7, 98.5)
6 months	95.5 (90.6, 100.0)	94.2 (91.1, 97.2)
9 months	95.5 (90.6, 100.0)	92.8 (88.8, 96.8)
12 months	95.5 (90.6, 100.0)	92.8 (88.8, 96.8)
18 months	NE (NE, NE)	92.8 (88.8, 96.8)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	4 (2.2)	10 (2.6)
Number of Subjects Censored, n (%)	181 (97.8)	370 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.155 (0.594)
95% CI		(0.361, 3.700)
Log-rank p-value		0.894

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (95.2, 100.0)	97.2 (95.5, 98.9)
6 months	97.6 (95.2, 100.0)	97.2 (95.5, 98.9)
9 months	97.6 (95.2, 100.0)	97.2 (95.5, 98.9)
12 months	97.6 (95.2, 100.0)	97.2 (95.5, 98.9)
18 months	NE (NE, NE)	97.2 (95.5, 98.9)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	2 (1.1)	11 (2.9)
Number of Subjects Censored, n (%)	183 (98.9)	369 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.193 (0.777)
95% CI		(0.479, 10.045)
Log-rank p-value		0.301

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (97.4, 100.0)	97.1 (95.3, 98.9)
6 months	98.9 (97.4, 100.0)	97.1 (95.3, 98.9)
9 months	98.9 (97.4, 100.0)	95.7 (92.3, 99.0)
12 months	98.9 (97.4, 100.0)	95.7 (92.3, 99.0)
18 months	NE (NE, NE)	95.7 (92.3, 99.0)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	0	14 (3.7)
Number of Subjects Censored, n (%)	185 (100.0)	366 (96.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.020

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.9 (95.2, 98.7)
6 months	100.0 (100.0, 100.0)	95.1 (92.3, 97.9)
9 months	100.0 (100.0, 100.0)	95.1 (92.3, 97.9)
12 months	100.0 (100.0, 100.0)	95.1 (92.3, 97.9)
18 months	NE (NE, NE)	95.1 (92.3, 97.9)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	3 (1.6)	11 (2.9)
Number of Subjects Censored, n (%)	182 (98.4)	369 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.428 (0.658)
95% CI		(0.393, 5.189)
Log-rank p-value		0.618

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.1, 100.0)	97.2 (95.4, 98.9)
6 months	97.8 (95.1, 100.0)	97.2 (95.4, 98.9)
9 months	97.8 (95.1, 100.0)	96.2 (93.8, 98.7)
12 months	97.8 (95.1, 100.0)	96.2 (93.8, 98.7)
18 months	NE (NE, NE)	96.2 (93.8, 98.7)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	2 (1.1)	9 (2.4)
Number of Subjects Censored, n (%)	183 (98.9)	371 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.647 (0.793)
95% CI		(0.348, 7.797)
Log-rank p-value		0.534

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (97.4, 100.0)	98.0 (96.6, 99.5)
6 months	98.9 (97.4, 100.0)	97.3 (95.2, 99.3)
9 months	98.9 (97.4, 100.0)	96.4 (93.7, 99.1)
12 months	98.9 (97.4, 100.0)	96.4 (93.7, 99.1)
18 months	NE (NE, NE)	96.4 (93.7, 99.1)
Median Follow-up Time (months)	2.79	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	2 (1.1)	11 (2.9)
Number of Subjects Censored, n (%)	183 (98.9)	369 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Median (95% CI)	10.18 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 10.2	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.256 (0.774)
95% CI		(0.495, 10.286)
Log-rank p-value		0.277

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.3, 100.0)	96.9 (95.1, 98.7)
6 months	99.4 (98.3, 100.0)	96.9 (95.1, 98.7)
9 months	99.4 (98.3, 100.0)	96.9 (95.1, 98.7)
12 months	0.0 (NE, NE)	96.9 (95.1, 98.7)
18 months	0.0 (NE, NE)	96.9 (95.1, 98.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	0	11 (2.9)
Number of Subjects Censored, n (%)	185 (100.0)	369 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.091

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.5 (97.1, 99.8)
6 months	100.0 (100.0, 100.0)	94.8 (91.6, 98.0)
9 months	100.0 (100.0, 100.0)	94.8 (91.6, 98.0)
12 months	100.0 (100.0, 100.0)	94.8 (91.6, 98.0)
18 months	NE (NE, NE)	94.8 (91.6, 98.0)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	56 (30.3)	158 (41.6)
Number of Subjects Censored, n (%)	129 (69.7)	222 (58.4)
Time to first TEAE (months)		
25% percentile (95% CI)	1.61 (0.95, 3.71)	1.61 (0.95, 1.81)
Median (95% CI)	NE (5.59, NE)	6.90 (5.78, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.179 (0.158)
95% CI		(0.865, 1.607)
Log-rank p-value		0.284

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	70.2 (63.4, 77.1)	62.3 (57.2, 67.3)
6 months	51.2 (32.0, 70.4)	55.3 (49.4, 61.2)
9 months	NE (NE, NE)	46.7 (39.4, 54.0)
12 months	NE (NE, NE)	46.7 (39.4, 54.0)
18 months	NE (NE, NE)	46.7 (39.4, 54.0)
Median Follow-up Time (months)	2.46	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	18 (9.7)	46 (12.1)
Number of Subjects Censored, n (%)	167 (90.3)	334 (87.9)
Time to first TEAE (months)		
25% percentile (95% CI)	5.82 (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.82, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.962 (0.284)
95% CI		(0.552, 1.678)
Log-rank p-value		0.820

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.6 (84.7, 94.5)	89.2 (86.0, 92.5)
6 months	72.8 (50.7, 95.0)	85.4 (81.1, 89.8)
9 months	NE (NE, NE)	83.1 (77.6, 88.5)
12 months	NE (NE, NE)	83.1 (77.6, 88.5)
18 months	NE (NE, NE)	83.1 (77.6, 88.5)
Median Follow-up Time (months)	2.73	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	9 (4.9)	37 (9.7)
Number of Subjects Censored, n (%)	176 (95.1)	343 (90.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.535 (0.379)
95% CI		(0.731, 3.224)
Log-rank p-value		0.258

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (92.4, 98.5)	91.4 (88.4, 94.4)
6 months	88.7 (75.5, 100.0)	89.2 (85.6, 92.8)
9 months	NE (NE, NE)	86.0 (80.9, 91.0)
12 months	NE (NE, NE)	86.0 (80.9, 91.0)
18 months	NE (NE, NE)	86.0 (80.9, 91.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	8 (4.3)	38 (10.0)
Number of Subjects Censored, n (%)	177 (95.7)	342 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.725 (0.396)
95% CI		(0.793, 3.750)
Log-rank p-value		0.152

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.1 (93.3, 98.9)	91.9 (89.0, 94.7)
6 months	89.2 (76.0, 100.0)	89.1 (85.4, 92.8)
9 months	NE (NE, NE)	85.0 (79.6, 90.3)
12 months	NE (NE, NE)	85.0 (79.6, 90.3)
18 months	NE (NE, NE)	85.0 (79.6, 90.3)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	11 (5.9)	31 (8.2)
Number of Subjects Censored, n (%)	174 (94.1)	349 (91.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.031 (0.358)
95% CI		(0.512, 2.078)
Log-rank p-value		0.994

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.9 (90.4, 97.4)	93.6 (91.0, 96.1)
6 months	93.9 (90.4, 97.4)	90.5 (87.0, 94.0)
9 months	93.9 (90.4, 97.4)	88.2 (83.5, 92.8)
12 months	93.9 (90.4, 97.4)	88.2 (83.5, 92.8)
18 months	NE (NE, NE)	88.2 (83.5, 92.8)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	3 (1.6)	31 (8.2)
Number of Subjects Censored, n (%)	182 (98.4)	349 (91.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.318 (0.610)
95% CI		(1.306, 14.272)
Log-rank p-value		0.012

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.8, 100.0)	92.7 (89.9, 95.4)
6 months	95.7 (89.9, 100.0)	91.2 (87.8, 94.6)
9 months	95.7 (89.9, 100.0)	87.3 (81.5, 93.1)
12 months	95.7 (89.9, 100.0)	87.3 (81.5, 93.1)
18 months	NE (NE, NE)	87.3 (81.5, 93.1)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	8 (4.3)	20 (5.3)
Number of Subjects Censored, n (%)	177 (95.7)	360 (94.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.012 (0.425)
95% CI		(0.440, 2.329)
Log-rank p-value		0.988

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (91.4, 98.4)	95.3 (93.0, 97.5)
6 months	94.9 (91.4, 98.4)	94.1 (91.4, 96.8)
9 months	94.9 (91.4, 98.4)	93.2 (90.0, 96.4)
12 months	94.9 (91.4, 98.4)	93.2 (90.0, 96.4)
18 months	NE (NE, NE)	93.2 (90.0, 96.4)
Median Follow-up Time (months)	2.79	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	2 (1.1)	22 (5.8)
Number of Subjects Censored, n (%)	183 (98.9)	358 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	7.43 (7.43, NE)	NE (NE, NE)
Median (95% CI)	7.43 (7.43, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (7.43, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.407 (0.743)
95% CI		(1.027, 18.912)
Log-rank p-value		0.029

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.4, 100.0)	94.7 (92.3, 97.0)
6 months	99.5 (98.4, 100.0)	93.1 (90.1, 96.0)
9 months	NE (NE, NE)	93.1 (90.1, 96.0)
12 months	NE (NE, NE)	93.1 (90.1, 96.0)
18 months	NE (NE, NE)	93.1 (90.1, 96.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	4 (2.2)	18 (4.7)
Number of Subjects Censored, n (%)	181 (97.8)	362 (95.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.597 (0.561)
95% CI		(0.532, 4.798)
Log-rank p-value		0.447

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (95.9, 100.0)	96.1 (94.0, 98.1)
6 months	95.3 (89.5, 100.0)	94.3 (91.4, 97.1)
9 months	95.3 (89.5, 100.0)	93.4 (90.1, 96.7)
12 months	95.3 (89.5, 100.0)	93.4 (90.1, 96.7)
18 months	NE (NE, NE)	93.4 (90.1, 96.7)
Median Follow-up Time (months)	2.79	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	1 (0.5)	12 (3.2)
Number of Subjects Censored, n (%)	184 (99.5)	368 (96.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.675 (1.047)
95% CI		(0.601, 36.378)
Log-rank p-value		0.104

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.3, 100.0)	97.1 (95.4, 98.9)
6 months	99.4 (98.3, 100.0)	96.6 (94.5, 98.6)
9 months	99.4 (98.3, 100.0)	95.4 (92.3, 98.5)
12 months	99.4 (98.3, 100.0)	95.4 (92.3, 98.5)
18 months	NE (NE, NE)	95.4 (92.3, 98.5)
Median Follow-up Time (months)	2.83	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	2 (1.1)	10 (2.6)
Number of Subjects Censored, n (%)	183 (98.9)	370 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.094 (0.782)
95% CI		(0.453, 9.689)
Log-rank p-value		0.336

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (97.3, 100.0)	97.4 (95.8, 99.1)
6 months	98.9 (97.3, 100.0)	97.4 (95.8, 99.1)
9 months	98.9 (97.3, 100.0)	96.2 (93.4, 99.1)
12 months	98.9 (97.3, 100.0)	96.2 (93.4, 99.1)
18 months	NE (NE, NE)	96.2 (93.4, 99.1)
Median Follow-up Time (months)	2.83	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	48 (25.9)	156 (41.1)
Number of Subjects Censored, n (%)	137 (74.1)	224 (58.9)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (1.02, NE)	0.69 (0.69, 1.12)
Median (95% CI)	NE (NE, NE)	9.69 (6.41, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.522 (0.167)
95% CI		(1.097, 2.110)
Log-rank p-value		0.014

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.4 (65.6, 79.1)	63.1 (58.2, 68.0)
6 months	72.4 (65.6, 79.1)	57.2 (51.6, 62.8)
9 months	72.4 (65.6, 79.1)	53.2 (46.7, 59.7)
12 months	72.4 (65.6, 79.1)	41.9 (28.9, 55.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.04	2.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	9 (4.9)	62 (16.3)
Number of Subjects Censored, n (%)	176 (95.1)	318 (83.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.508 (0.359)
95% CI		(1.737, 7.083)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (91.6, 98.1)	83.7 (80.0, 87.5)
6 months	94.9 (91.6, 98.1)	83.3 (79.4, 87.1)
9 months	94.9 (91.6, 98.1)	83.3 (79.4, 87.1)
12 months	94.9 (91.6, 98.1)	83.3 (79.4, 87.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.33

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	20 (10.8)	41 (10.8)
Number of Subjects Censored, n (%)	165 (89.2)	339 (89.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	14.32 (10.28, NE)
Median (95% CI)	NE (NE, NE)	NE (14.32, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (14.32, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.760 (0.279)
95% CI		(0.440, 1.312)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.5 (83.8, 93.3)	91.4 (88.5, 94.3)
6 months	88.5 (83.8, 93.3)	88.2 (84.4, 92.0)
9 months	88.5 (83.8, 93.3)	86.5 (82.1, 90.9)
12 months	88.5 (83.8, 93.3)	82.2 (72.9, 91.5)
18 months	NE (NE, NE)	61.6 (26.1, 97.2)
Median Follow-up Time (months)	2.73	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	18 (9.7)	36 (9.5)
Number of Subjects Censored, n (%)	167 (90.3)	344 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.856 (0.293)
95% CI		(0.482, 1.519)
Log-rank p-value		0.644

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.4 (84.8, 94.1)	91.2 (88.3, 94.2)
6 months	89.4 (84.8, 94.1)	90.2 (87.0, 93.4)
9 months	89.4 (84.8, 94.1)	89.3 (85.6, 93.0)
12 months	89.4 (84.8, 94.1)	82.4 (69.1, 95.8)
18 months	NE (NE, NE)	82.4 (69.1, 95.8)
Median Follow-up Time (months)	2.56	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	3 (1.6)	16 (4.2)
Number of Subjects Censored, n (%)	182 (98.4)	364 (95.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.493 (0.630)
95% CI		(0.725, 8.568)
Log-rank p-value		0.143

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.5, 100.0)	95.6 (93.5, 97.7)
6 months	98.4 (96.5, 100.0)	95.6 (93.5, 97.7)
9 months	98.4 (96.5, 100.0)	95.6 (93.5, 97.7)
12 months	98.4 (96.5, 100.0)	95.6 (93.5, 97.7)
18 months	NE (NE, NE)	95.6 (93.5, 97.7)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	2 (1.1)	9 (2.4)
Number of Subjects Censored, n (%)	183 (98.9)	371 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.612 (0.796)
95% CI		(0.338, 7.681)
Log-rank p-value		0.571

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (97.1, 100.0)	98.1 (96.8, 99.5)
6 months	98.8 (97.1, 100.0)	98.1 (96.8, 99.5)
9 months	98.8 (97.1, 100.0)	96.0 (92.7, 99.3)
12 months	98.8 (97.1, 100.0)	96.0 (92.7, 99.3)
18 months	NE (NE, NE)	96.0 (92.7, 99.3)
Median Follow-up Time (months)	2.79	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Vascular disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	31 (16.8)	154 (40.5)
Number of Subjects Censored, n (%)	154 (83.2)	226 (59.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.61, NE)	0.92 (0.69, 1.18)
Median (95% CI)	NE (NE, NE)	NE (6.44, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.518 (0.198)
95% CI		(1.709, 3.708)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Vascular disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.6 (76.9, 88.3)	60.6 (55.5, 65.6)
6 months	79.5 (71.5, 87.6)	56.9 (51.3, 62.4)
9 months	NE (NE, NE)	53.0 (46.2, 59.7)
12 months	NE (NE, NE)	53.0 (46.2, 59.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.40	2.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	18 (9.7)	143 (37.6)
Number of Subjects Censored, n (%)	167 (90.3)	237 (62.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.95 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	NE (7.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.132 (0.251)
95% CI		(2.528, 6.753)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.5 (84.9, 94.1)	63.0 (58.0, 68.0)
6 months	89.5 (84.9, 94.1)	60.7 (55.4, 66.0)
9 months	NE (NE, NE)	56.7 (50.1, 63.4)
12 months	NE (NE, NE)	56.7 (50.1, 63.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.63	2.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	39 (21.1)	135 (35.5)
Number of Subjects Censored, n (%)	146 (78.9)	245 (64.5)
Time to first TEAE (months)		
25% percentile (95% CI)	3.71 (1.87, NE)	1.61 (0.95, 1.87)
Median (95% CI)	NE (5.59, NE)	NE (8.64, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.569 (0.183)
95% CI		(1.095, 2.247)
Log-rank p-value		0.009

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.0 (72.7, 85.2)	65.9 (61.0, 70.8)
6 months	65.2 (47.9, 82.4)	62.3 (56.8, 67.7)
9 months	NE (NE, NE)	57.2 (49.5, 65.0)
12 months	NE (NE, NE)	53.4 (43.2, 63.6)
18 months	NE (NE, NE)	53.4 (43.2, 63.6)
Median Follow-up Time (months)	2.46	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	16 (8.6)	40 (10.5)
Number of Subjects Censored, n (%)	169 (91.4)	340 (89.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.004 (0.300)
95% CI		(0.558, 1.808)
Log-rank p-value		0.899

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.0 (86.8, 95.2)	90.5 (87.5, 93.6)
6 months	91.0 (86.8, 95.2)	87.9 (84.1, 91.6)
9 months	91.0 (86.8, 95.2)	87.0 (83.0, 91.1)
12 months	91.0 (86.8, 95.2)	87.0 (83.0, 91.1)
18 months	NE (NE, NE)	87.0 (83.0, 91.1)
Median Follow-up Time (months)	2.76	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	6 (3.2)	46 (12.1)
Number of Subjects Censored, n (%)	179 (96.8)	334 (87.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (7.98, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.026 (0.438)
95% CI		(1.283, 7.136)
Log-rank p-value		0.008

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (94.7, 99.6)	89.5 (86.3, 92.7)
6 months	90.2 (76.9, 100.0)	86.4 (82.2, 90.6)
9 months	NE (NE, NE)	82.1 (75.8, 88.3)
12 months	NE (NE, NE)	82.1 (75.8, 88.3)
18 months	NE (NE, NE)	82.1 (75.8, 88.3)
Median Follow-up Time (months)	2.79	3.56

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	3 (1.6)	24 (6.3)
Number of Subjects Censored, n (%)	182 (98.4)	356 (93.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.372 (0.615)
95% CI		(1.011, 11.248)
Log-rank p-value		0.030

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.4, 100.0)	93.7 (91.2, 96.2)
6 months	93.8 (86.1, 100.0)	93.0 (90.2, 95.8)
9 months	93.8 (86.1, 100.0)	93.0 (90.2, 95.8)
12 months	93.8 (86.1, 100.0)	93.0 (90.2, 95.8)
18 months	NE (NE, NE)	93.0 (90.2, 95.8)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	5 (2.7)	14 (3.7)
Number of Subjects Censored, n (%)	180 (97.3)	366 (96.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.203 (0.526)
95% CI		(0.429, 3.370)
Log-rank p-value		0.696

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (94.7, 99.6)	96.4 (94.5, 98.3)
6 months	97.2 (94.7, 99.6)	95.5 (93.0, 98.1)
9 months	97.2 (94.7, 99.6)	95.5 (93.0, 98.1)
12 months	97.2 (94.7, 99.6)	95.5 (93.0, 98.1)
18 months	NE (NE, NE)	95.5 (93.0, 98.1)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	2 (1.1)	11 (2.9)
Number of Subjects Censored, n (%)	183 (98.9)	369 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.840 (0.782)
95% CI		(0.397, 8.527)
Log-rank p-value		0.418

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (97.4, 100.0)	97.8 (96.3, 99.3)
6 months	98.9 (97.4, 100.0)	97.1 (95.0, 99.2)
9 months	98.9 (97.4, 100.0)	93.1 (87.2, 99.0)
12 months	98.9 (97.4, 100.0)	93.1 (87.2, 99.0)
18 months	NE (NE, NE)	93.1 (87.2, 99.0)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	0	10 (2.6)
Number of Subjects Censored, n (%)	185 (100.0)	370 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.035

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.1 (95.4, 98.9)
6 months	100.0 (100.0, 100.0)	97.1 (95.4, 98.9)
9 months	100.0 (100.0, 100.0)	97.1 (95.4, 98.9)
12 months	100.0 (100.0, 100.0)	97.1 (95.4, 98.9)
18 months	NE (NE, NE)	97.1 (95.4, 98.9)
Median Follow-up Time (months)	2.83	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	24 (13.0)	136 (35.8)
Number of Subjects Censored, n (%)	161 (87.0)	244 (64.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	1.58 (0.95, 1.84)
Median (95% CI)	NE (NE, NE)	13.14 (13.14, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.14, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.855 (0.223)
95% CI		(1.843, 4.423)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.1 (82.2, 92.0)	66.2 (61.3, 71.1)
6 months	84.0 (76.3, 91.6)	61.0 (55.4, 66.6)
9 months	84.0 (76.3, 91.6)	58.3 (51.8, 64.8)
12 months	84.0 (76.3, 91.6)	58.3 (51.8, 64.8)
18 months	NE (NE, NE)	29.2 (0.0, 69.7)
Median Follow-up Time (months)	2.60	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	6 (3.2)	79 (20.8)
Number of Subjects Censored, n (%)	179 (96.8)	301 (79.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	7.39 (3.65, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.625 (0.426)
95% CI		(2.875, 15.266)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.6 (94.0, 99.3)	81.1 (77.1, 85.1)
6 months	96.6 (94.0, 99.3)	76.5 (71.6, 81.4)
9 months	96.6 (94.0, 99.3)	74.9 (69.2, 80.6)
12 months	96.6 (94.0, 99.3)	74.9 (69.2, 80.6)
18 months	NE (NE, NE)	74.9 (69.2, 80.6)
Median Follow-up Time (months)	2.79	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	8 (4.3)	15 (3.9)
Number of Subjects Censored, n (%)	177 (95.7)	365 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.854 (0.440)
95% CI		(0.360, 2.024)
Log-rank p-value		0.730

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (92.6, 98.6)	95.8 (93.7, 97.9)
6 months	95.6 (92.6, 98.6)	95.8 (93.7, 97.9)
9 months	95.6 (92.6, 98.6)	95.8 (93.7, 97.9)
12 months	95.6 (92.6, 98.6)	95.8 (93.7, 97.9)
18 months	NE (NE, NE)	95.8 (93.7, 97.9)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	3 (1.6)	10 (2.6)
Number of Subjects Censored, n (%)	182 (98.4)	370 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.283 (0.666)
95% CI		(0.348, 4.731)
Log-rank p-value		0.713

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (97.2, 100.0)	97.5 (95.9, 99.1)
6 months	95.9 (90.1, 100.0)	97.0 (95.1, 98.9)
9 months	95.9 (90.1, 100.0)	97.0 (95.1, 98.9)
12 months	95.9 (90.1, 100.0)	97.0 (95.1, 98.9)
18 months	NE (NE, NE)	97.0 (95.1, 98.9)
Median Follow-up Time (months)	2.79	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Nervous system disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	30 (16.2)	96 (25.3)
Number of Subjects Censored, n (%)	155 (83.8)	284 (74.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.57 (2.37, 11.10)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.344 (0.212)
95% CI		(0.888, 2.036)
Log-rank p-value		0.178

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Nervous system disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.1 (76.1, 88.0)	77.3 (72.9, 81.6)
6 months	82.1 (76.1, 88.0)	71.7 (66.4, 77.1)
9 months	82.1 (76.1, 88.0)	69.9 (64.1, 75.7)
12 months	82.1 (76.1, 88.0)	65.3 (54.9, 75.6)
18 months	NE (NE, NE)	65.3 (54.9, 75.6)
Median Follow-up Time (months)	2.56	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	9 (4.9)	35 (9.2)
Number of Subjects Censored, n (%)	176 (95.1)	345 (90.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.1, 13.0*	0.0, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.626 (0.378)
95% CI		(0.775, 3.411)
Log-rank p-value		0.197

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.5 (90.9, 98.1)	92.0 (89.2, 94.7)
6 months	94.5 (90.9, 98.1)	90.8 (87.7, 94.0)
9 months	94.5 (90.9, 98.1)	89.0 (85.1, 93.0)
12 months	94.5 (90.9, 98.1)	89.0 (85.1, 93.0)
18 months	NE (NE, NE)	89.0 (85.1, 93.0)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	5 (2.7)	7 (1.8)
Number of Subjects Censored, n (%)	180 (97.3)	373 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.626 (0.587)
95% CI		(0.198, 1.977)
Log-rank p-value		0.415

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (94.9, 99.6)	98.0 (96.6, 99.5)
6 months	97.2 (94.9, 99.6)	98.0 (96.6, 99.5)
9 months	97.2 (94.9, 99.6)	98.0 (96.6, 99.5)
12 months	97.2 (94.9, 99.6)	98.0 (96.6, 99.5)
18 months	NE (NE, NE)	98.0 (96.6, 99.5)
Median Follow-up Time (months)	2.79	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	4 (2.2)	10 (2.6)
Number of Subjects Censored, n (%)	181 (97.8)	370 (97.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.129 (0.594)
95% CI		(0.353, 3.617)
Log-rank p-value		0.871

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (95.4, 99.9)	97.3 (95.6, 98.9)
6 months	97.6 (95.4, 99.9)	97.3 (95.6, 98.9)
9 months	97.6 (95.4, 99.9)	97.3 (95.6, 98.9)
12 months	97.6 (95.4, 99.9)	97.3 (95.6, 98.9)
18 months	NE (NE, NE)	97.3 (95.6, 98.9)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	26 (14.1)	102 (26.8)
Number of Subjects Censored, n (%)	159 (85.9)	278 (73.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	3.68 (2.69, 5.55)
Median (95% CI)	NE (NE, NE)	13.60 (11.96, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.568 (0.222)
95% CI		(1.015, 2.424)
Log-rank p-value		0.056

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.8 (79.1, 90.4)	77.0 (72.6, 81.4)
6 months	81.6 (73.5, 89.7)	68.7 (63.0, 74.4)
9 months	81.6 (73.5, 89.7)	66.7 (60.6, 72.9)
12 months	81.6 (73.5, 89.7)	58.4 (42.2, 74.6)
18 months	NE (NE, NE)	38.9 (6.0, 71.9)
Median Follow-up Time (months)	2.56	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	11 (5.9)	70 (18.4)
Number of Subjects Censored, n (%)	174 (94.1)	310 (81.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.60 (5.06, NE)
Median (95% CI)	NE (NE, NE)	NE (13.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.2*, 13.0*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.579 (0.327)
95% CI		(1.359, 4.894)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.6 (89.9, 97.3)	83.7 (79.8, 87.6)
6 months	93.6 (89.9, 97.3)	78.4 (73.5, 83.3)
9 months	93.6 (89.9, 97.3)	76.3 (70.0, 82.6)
12 months	93.6 (89.9, 97.3)	76.3 (70.0, 82.6)
18 months	NE (NE, NE)	50.8 (9.9, 91.7)
Median Follow-up Time (months)	2.73	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	3 (1.6)	9 (2.4)
Number of Subjects Censored, n (%)	182 (98.4)	371 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.354 (0.671)
95% CI		(0.363, 5.043)
Log-rank p-value		0.705

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (96.5, 100.0)	97.8 (96.3, 99.3)
6 months	98.3 (96.5, 100.0)	97.3 (95.5, 99.1)
9 months	98.3 (96.5, 100.0)	97.3 (95.5, 99.1)
12 months	98.3 (96.5, 100.0)	97.3 (95.5, 99.1)
18 months	NE (NE, NE)	97.3 (95.5, 99.1)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Infections and infestations**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	24 (13.0)	81 (21.3)
Number of Subjects Censored, n (%)	161 (87.0)	299 (78.7)
Time to first TEAE (months)		
25% percentile (95% CI)	5.78 (4.34, NE)	5.91 (4.60, 7.69)
Median (95% CI)	NE (5.78, NE)	NE (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.144 (0.239)
95% CI		(0.716, 1.828)
Log-rank p-value		0.483

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Infections and infestations**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (82.4, 92.6)	83.8 (79.9, 87.7)
6 months	70.4 (49.7, 91.2)	74.5 (68.7, 80.3)
9 months	70.4 (49.7, 91.2)	64.1 (55.6, 72.7)
12 months	70.4 (49.7, 91.2)	57.7 (43.5, 71.9)
18 months	NE (NE, NE)	57.7 (43.5, 71.9)
Median Follow-up Time (months)	2.76	3.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	5 (2.7)	16 (4.2)
Number of Subjects Censored, n (%)	180 (97.3)	364 (95.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.930 (0.528)
95% CI		(0.330, 2.619)
Log-rank p-value		0.911

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (97.4, 100.0)	97.0 (95.2, 98.7)
6 months	88.7 (77.2, 100.0)	95.6 (93.0, 98.2)
9 months	88.7 (77.2, 100.0)	92.5 (88.2, 96.8)
12 months	88.7 (77.2, 100.0)	92.5 (88.2, 96.8)
18 months	NE (NE, NE)	92.5 (88.2, 96.8)
Median Follow-up Time (months)	2.79	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	5 (2.7)	12 (3.2)
Number of Subjects Censored, n (%)	180 (97.3)	368 (96.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.56, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.580 (0.559)
95% CI		(0.194, 1.733)
Log-rank p-value		0.357

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (95.0, 100.0)	98.5 (97.2, 99.8)
6 months	93.2 (84.7, 100.0)	95.7 (92.9, 98.5)
9 months	93.2 (84.7, 100.0)	94.7 (91.3, 98.1)
12 months	93.2 (84.7, 100.0)	87.9 (74.8, 100.0)
18 months	NE (NE, NE)	87.9 (74.8, 100.0)
Median Follow-up Time (months)	2.79	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	1 (0.5)	11 (2.9)
Number of Subjects Censored, n (%)	184 (99.5)	369 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.183 (1.048)
95% CI		(0.537, 32.603)
Log-rank p-value		0.126

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.4, 100.0)	97.0 (95.1, 98.9)
6 months	99.5 (98.4, 100.0)	96.2 (93.9, 98.6)
9 months	99.5 (98.4, 100.0)	96.2 (93.9, 98.6)
12 months	99.5 (98.4, 100.0)	96.2 (93.9, 98.6)
18 months	NE (NE, NE)	96.2 (93.9, 98.6)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	31 (16.8)	54 (14.2)
Number of Subjects Censored, n (%)	154 (83.2)	326 (85.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.79, NE)	NE (6.77, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.664 (0.230)
95% CI		(0.423, 1.042)
Log-rank p-value		0.094

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.8 (74.5, 87.0)	87.8 (84.4, 91.2)
6 months	80.8 (74.5, 87.0)	83.4 (78.9, 88.0)
9 months	80.8 (74.5, 87.0)	80.5 (75.0, 86.0)
12 months	80.8 (74.5, 87.0)	80.5 (75.0, 86.0)
18 months	NE (NE, NE)	80.5 (75.0, 86.0)
Median Follow-up Time (months)	2.46	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	25 (13.5)	29 (7.6)
Number of Subjects Censored, n (%)	160 (86.5)	351 (92.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.396 (0.282)
95% CI		(0.228, 0.689)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.0 (78.0, 89.9)	94.3 (91.8, 96.7)
6 months	84.0 (78.0, 89.9)	89.8 (85.7, 93.9)
9 months	84.0 (78.0, 89.9)	88.0 (83.3, 92.7)
12 months	84.0 (78.0, 89.9)	88.0 (83.3, 92.7)
18 months	NE (NE, NE)	88.0 (83.3, 92.7)
Median Follow-up Time (months)	2.60	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	2 (1.1)	21 (5.5)
Number of Subjects Censored, n (%)	183 (98.9)	359 (94.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.850 (0.740)
95% CI		(1.136, 20.701)
Log-rank p-value		0.019

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (97.2, 100.0)	94.3 (91.9, 96.7)
6 months	98.8 (97.2, 100.0)	94.3 (91.9, 96.7)
9 months	98.8 (97.2, 100.0)	94.3 (91.9, 96.7)
12 months	98.8 (97.2, 100.0)	94.3 (91.9, 96.7)
18 months	NE (NE, NE)	94.3 (91.9, 96.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Endocrine disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	1 (0.5)	81 (21.3)
Number of Subjects Censored, n (%)	184 (99.5)	299 (78.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.68 (4.07, 6.90)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		31.037 (1.007)
95% CI		(4.312, 223.411)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Endocrine disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.3, 100.0)	82.7 (78.7, 86.7)
6 months	99.4 (98.3, 100.0)	71.7 (65.4, 78.0)
9 months	99.4 (98.3, 100.0)	68.3 (61.3, 75.4)
12 months	99.4 (98.3, 100.0)	64.9 (55.5, 74.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.07

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	1 (0.5)	75 (19.7)
Number of Subjects Censored, n (%)	184 (99.5)	305 (80.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.98 (5.52, 9.33)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		27.857 (1.008)
95% CI		(3.865, 200.799)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.3, 100.0)	84.4 (80.6, 88.2)
6 months	99.4 (98.3, 100.0)	74.1 (68.0, 80.2)
9 months	99.4 (98.3, 100.0)	69.2 (61.8, 76.6)
12 months	99.4 (98.3, 100.0)	65.9 (56.4, 75.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Psychiatric disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	12 (6.5)	49 (12.9)
Number of Subjects Censored, n (%)	173 (93.5)	331 (87.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.528 (0.326)
95% CI		(0.806, 2.896)
Log-rank p-value		0.163

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Psychiatric disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.8 (90.3, 97.4)	88.9 (85.6, 92.3)
6 months	91.7 (86.4, 97.1)	83.4 (78.7, 88.0)
9 months	91.7 (86.4, 97.1)	82.4 (77.4, 87.4)
12 months	91.7 (86.4, 97.1)	82.4 (77.4, 87.4)
18 months	NE (NE, NE)	82.4 (77.4, 87.4)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	8 (4.3)	24 (6.3)
Number of Subjects Censored, n (%)	177 (95.7)	356 (93.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.073 (0.414)
95% CI		(0.477, 2.414)
Log-rank p-value		0.747

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (92.4, 98.5)	94.5 (92.0, 97.0)
6 months	95.5 (92.4, 98.5)	92.0 (88.7, 95.3)
9 months	95.5 (92.4, 98.5)	90.9 (87.0, 94.8)
12 months	95.5 (92.4, 98.5)	90.9 (87.0, 94.8)
18 months	NE (NE, NE)	90.9 (87.0, 94.8)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	2 (1.1)	8 (2.1)
Number of Subjects Censored, n (%)	183 (98.9)	372 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.547 (0.801)
95% CI		(0.322, 7.431)
Log-rank p-value		0.671

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.1, 100.0)	97.8 (96.2, 99.4)
6 months	97.2 (92.8, 100.0)	97.1 (95.1, 99.2)
9 months	97.2 (92.8, 100.0)	97.1 (95.1, 99.2)
12 months	97.2 (92.8, 100.0)	97.1 (95.1, 99.2)
18 months	NE (NE, NE)	97.1 (95.1, 99.2)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	1 (0.5)	7 (1.8)
Number of Subjects Censored, n (%)	184 (99.5)	373 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.322 (1.079)
95% CI		(0.280, 19.244)
Log-rank p-value		0.446

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.3, 100.0)	98.6 (97.3, 99.8)
6 months	99.4 (98.3, 100.0)	97.3 (95.2, 99.5)
9 months	99.4 (98.3, 100.0)	97.3 (95.2, 99.5)
12 months	99.4 (98.3, 100.0)	97.3 (95.2, 99.5)
18 months	NE (NE, NE)	97.3 (95.2, 99.5)
Median Follow-up Time (months)	2.83	3.96

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	23 (12.4)	47 (12.4)
Number of Subjects Censored, n (%)	162 (87.6)	333 (87.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.790 (0.258)
95% CI		(0.476, 1.309)
Log-rank p-value		0.385

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (82.6, 92.4)	88.5 (85.2, 91.9)
6 months	85.5 (79.4, 91.7)	84.4 (80.0, 88.9)
9 months	85.5 (79.4, 91.7)	84.4 (80.0, 88.9)
12 months	85.5 (79.4, 91.7)	84.4 (80.0, 88.9)
18 months	NE (NE, NE)	84.4 (80.0, 88.9)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	3 (1.6)	18 (4.7)
Number of Subjects Censored, n (%)	182 (98.4)	362 (95.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.180 (0.628)
95% CI		(0.637, 7.465)
Log-rank p-value		0.214

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (96.0, 100.0)	95.2 (92.9, 97.5)
6 months	98.1 (96.0, 100.0)	93.9 (91.0, 96.8)
9 months	98.1 (96.0, 100.0)	93.9 (91.0, 96.8)
12 months	98.1 (96.0, 100.0)	93.9 (91.0, 96.8)
18 months	NE (NE, NE)	93.9 (91.0, 96.8)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3J
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
>3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Number of Subjects with Events, n (%)	2 (1.1)	13 (3.4)
Number of Subjects Censored, n (%)	183 (98.9)	367 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.669 (0.765)
95% CI		(0.596, 11.946)
Log-rank p-value		0.195

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
<=3

Statistics	Placebo + BSC N=185	Fruquintinib + BSC N=380
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (97.4, 100.0)	96.9 (95.1, 98.7)
6 months	98.9 (97.4, 100.0)	95.7 (93.2, 98.2)
9 months	98.9 (97.4, 100.0)	95.7 (93.2, 98.2)
12 months	98.9 (97.4, 100.0)	95.7 (93.2, 98.2)
18 months	NE (NE, NE)	95.7 (93.2, 98.2)
Median Follow-up Time (months)	2.83	3.86

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	30 (46.9)	69 (55.6)
Number of Subjects Censored, n (%)	34 (53.1)	55 (44.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.82 (0.49, 1.35)	0.69 (0.66, 0.95)
Median (95% CI)	3.19 (1.41, NE)	3.06 (1.41, 6.97)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Min, Max	0.0, 5.6*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.231 (0.222)
95% CI		(0.796, 1.903)
Log-rank p-value		0.376

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	53.9 (41.5, 66.3)	50.3 (41.5, 59.2)
6 months	NE (NE, NE)	40.5 (30.7, 50.3)
9 months	NE (NE, NE)	37.4 (26.6, 48.2)
12 months	NE (NE, NE)	37.4 (26.6, 48.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.92	2.37

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	12 (18.8)	28 (22.6)
Number of Subjects Censored, n (%)	52 (81.3)	96 (77.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.92, NE)	NE (1.61, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.198 (0.348)
95% CI		(0.606, 2.369)
Log-rank p-value		0.597

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.9 (71.2, 90.6)	78.3 (70.9, 85.7)
6 months	NE (NE, NE)	75.9 (68.0, 83.8)
9 months	NE (NE, NE)	75.9 (68.0, 83.8)
12 months	NE (NE, NE)	75.9 (68.0, 83.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	11 (17.2)	22 (17.7)
Number of Subjects Censored, n (%)	53 (82.8)	102 (82.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.35, NE)	NE (4.60, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.921 (0.377)
95% CI		(0.440, 1.929)
Log-rank p-value		0.808

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.4 (73.0, 91.9)	83.6 (77.0, 90.2)
6 months	NE (NE, NE)	81.9 (74.6, 89.1)
9 months	NE (NE, NE)	78.5 (68.9, 88.0)
12 months	NE (NE, NE)	78.5 (68.9, 88.0)
18 months	NE (NE, NE)	78.5 (68.9, 88.0)
Median Follow-up Time (months)	2.83	3.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	4 (6.3)	5 (4.0)
Number of Subjects Censored, n (%)	60 (93.8)	119 (96.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.538 (0.711)
95% CI		(0.133, 2.169)
Log-rank p-value		0.403

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.7 (85.7, 99.8)	96.8 (93.7, 99.9)
6 months	NE (NE, NE)	96.8 (93.7, 99.9)
9 months	NE (NE, NE)	96.8 (93.7, 99.9)
12 months	NE (NE, NE)	84.7 (62.3, 100.0)
18 months	NE (NE, NE)	84.7 (62.3, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	1 (1.6)	17 (13.7)
Number of Subjects Censored, n (%)	63 (98.4)	107 (86.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.24 (7.26, NE)
Median (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.24, NE)
Min, Max	0.7, 5.6*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		8.683 (1.034)
95% CI		(1.144, 65.907)
Log-rank p-value		0.010

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (95.4, 100.0)	88.6 (83.0, 94.2)
6 months	NE (NE, NE)	87.1 (80.8, 93.4)
9 months	NE (NE, NE)	83.3 (73.9, 92.7)
12 months	NE (NE, NE)	83.3 (73.9, 92.7)
18 months	NE (NE, NE)	41.6 (0.0, 99.6)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	6 (9.4)	9 (7.3)
Number of Subjects Censored, n (%)	58 (90.6)	115 (92.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.19, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.561 (0.554)
95% CI		(0.190, 1.663)
Log-rank p-value		0.285

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.0 (83.4, 98.6)	95.1 (91.3, 98.9)
6 months	NE (NE, NE)	90.3 (83.9, 96.8)
9 months	NE (NE, NE)	90.3 (83.9, 96.8)
12 months	NE (NE, NE)	90.3 (83.9, 96.8)
18 months	NE (NE, NE)	90.3 (83.9, 96.8)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	4 (6.3)	5 (4.0)
Number of Subjects Censored, n (%)	60 (93.8)	119 (96.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.99, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 5.6*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.472 (0.716)
95% CI		(0.116, 1.920)
Log-rank p-value		0.300

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.0 (86.2, 99.8)	96.6 (93.2, 99.9)
6 months	NE (NE, NE)	96.6 (93.2, 99.9)
9 months	NE (NE, NE)	96.6 (93.2, 99.9)
12 months	NE (NE, NE)	89.1 (74.8, 100.0)
18 months	NE (NE, NE)	89.1 (74.8, 100.0)
Median Follow-up Time (months)	2.83	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	1 (1.6)	3 (2.4)
Number of Subjects Censored, n (%)	63 (98.4)	121 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.05, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.000 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.025

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (94.3, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	95.7 (87.3, 100.0)
12 months	NE (NE, NE)	83.4 (65.7, 100.0)
18 months	NE (NE, NE)	83.4 (65.7, 100.0)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	1 (1.6)	3 (2.4)
Number of Subjects Censored, n (%)	63 (98.4)	121 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.580 (1.274)
95% CI		(0.048, 7.040)
Log-rank p-value		0.567

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (94.8, 100.0)	99.0 (97.0, 100.0)
6 months	NE (NE, NE)	97.2 (93.2, 100.0)
9 months	NE (NE, NE)	93.0 (84.0, 100.0)
12 months	NE (NE, NE)	93.0 (84.0, 100.0)
18 months	NE (NE, NE)	93.0 (84.0, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	0	2 (1.6)
Number of Subjects Censored, n (%)	64 (100.0)	122 (98.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.57, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.429

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.2 (97.6, 100.0)
6 months	NE (NE, NE)	99.2 (97.6, 100.0)
9 months	NE (NE, NE)	94.0 (83.9, 100.0)
12 months	NE (NE, NE)	94.0 (83.9, 100.0)
18 months	NE (NE, NE)	94.0 (83.9, 100.0)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	35 (54.7)	82 (66.1)
Number of Subjects Censored, n (%)	29 (45.3)	42 (33.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.44 (0.13, 0.69)	0.69 (0.46, 0.69)
Median (95% CI)	1.61 (0.72, NE)	1.64 (0.95, 3.55)
75% percentile (95% CI)	NE (NE, NE)	6.47 (4.63, 7.79)
Min, Max	0.0, 5.6*	0.0, 10.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.018 (0.209)
95% CI		(0.676, 1.532)
Log-rank p-value		0.624

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	44.1 (31.6, 56.5)	42.8 (34.0, 51.6)
6 months	NE (NE, NE)	28.4 (18.0, 38.7)
9 months	NE (NE, NE)	9.7 (0.0, 21.2)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.49	1.46

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	7 (10.9)	24 (19.4)
Number of Subjects Censored, n (%)	57 (89.1)	100 (80.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	6.47 (3.71, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.413 (0.444)
95% CI		(0.592, 3.372)
Log-rank p-value		0.426

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.1 (81.4, 96.7)	86.0 (79.8, 92.2)
6 months	NE (NE, NE)	75.8 (65.4, 86.1)
9 months	NE (NE, NE)	68.7 (55.4, 82.0)
12 months	NE (NE, NE)	68.7 (55.4, 82.0)
18 months	NE (NE, NE)	68.7 (55.4, 82.0)
Median Follow-up Time (months)	2.79	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	12 (18.8)	17 (13.7)
Number of Subjects Censored, n (%)	52 (81.3)	107 (86.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.72, NE)	9.20 (4.63, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.433 (0.409)
95% CI		(0.194, 0.967)
Log-rank p-value		0.070

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.9 (71.1, 90.6)	91.0 (85.9, 96.1)
6 months	NE (NE, NE)	84.5 (76.7, 92.3)
9 months	NE (NE, NE)	84.5 (76.7, 92.3)
12 months	NE (NE, NE)	74.2 (59.2, 89.2)
18 months	NE (NE, NE)	74.2 (59.2, 89.2)
Median Follow-up Time (months)	2.79	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	12 (18.8)	25 (20.2)
Number of Subjects Censored, n (%)	52 (81.3)	99 (79.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.28, NE)	7.75 (3.68, NE)
Median (95% CI)	NE (NE, NE)	NE (9.23, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.2, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.709 (0.378)
95% CI		(0.338, 1.486)
Log-rank p-value		0.498

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.8 (70.9, 90.6)	85.7 (79.3, 92.0)
6 months	NE (NE, NE)	78.5 (69.5, 87.6)
9 months	NE (NE, NE)	71.6 (59.2, 84.0)
12 months	NE (NE, NE)	66.8 (52.2, 81.5)
18 months	NE (NE, NE)	53.5 (27.3, 79.7)
Median Follow-up Time (months)	2.83	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	4 (6.3)	18 (14.5)
Number of Subjects Censored, n (%)	60 (93.8)	106 (85.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.70, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.720 (0.567)
95% CI		(0.567, 5.222)
Log-rank p-value		0.357

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.8 (87.8, 99.7)	87.6 (81.5, 93.8)
6 months	NE (NE, NE)	81.1 (71.9, 90.3)
9 months	NE (NE, NE)	77.4 (66.2, 88.7)
12 months	NE (NE, NE)	77.4 (66.2, 88.7)
18 months	NE (NE, NE)	77.4 (66.2, 88.7)
Median Follow-up Time (months)	2.83	3.43

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	11 (17.2)	13 (10.5)
Number of Subjects Censored, n (%)	53 (82.8)	111 (89.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.58, NE)	NE (7.10, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.344 (0.460)
95% CI		(0.139, 0.847)
Log-rank p-value		0.024

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.5 (73.1, 91.9)	94.3 (90.2, 98.4)
6 months	NE (NE, NE)	89.9 (83.6, 96.2)
9 months	NE (NE, NE)	81.7 (69.5, 93.9)
12 months	NE (NE, NE)	75.9 (60.1, 91.7)
18 months	NE (NE, NE)	75.9 (60.1, 91.7)
Median Follow-up Time (months)	2.83	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	1 (1.6)	12 (9.7)
Number of Subjects Censored, n (%)	63 (98.4)	112 (90.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.87, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.048 (1.047)
95% CI		(0.648, 39.288)
Log-rank p-value		0.101

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (95.1, 100.0)	91.8 (87.0, 96.7)
6 months	NE (NE, NE)	90.5 (85.1, 96.0)
9 months	NE (NE, NE)	86.8 (77.9, 95.7)
12 months	NE (NE, NE)	86.8 (77.9, 95.7)
18 months	NE (NE, NE)	86.8 (77.9, 95.7)
Median Follow-up Time (months)	2.83	3.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	2 (3.1)	11 (8.9)
Number of Subjects Censored, n (%)	62 (96.9)	113 (91.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.79, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.885 (0.776)
95% CI		(0.630, 13.205)
Log-rank p-value		0.157

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (92.6, 100.0)	91.7 (86.7, 96.6)
6 months	NE (NE, NE)	91.7 (86.7, 96.6)
9 months	NE (NE, NE)	87.1 (77.1, 97.0)
12 months	NE (NE, NE)	87.1 (77.1, 97.0)
18 months	NE (NE, NE)	87.1 (77.1, 97.0)
Median Follow-up Time (months)	2.83	3.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	1 (1.6)	4 (3.2)
Number of Subjects Censored, n (%)	63 (98.4)	120 (96.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9, 5.6*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.606 (1.141)
95% CI		(0.171, 15.046)
Log-rank p-value		0.658

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (95.4, 100.0)	97.5 (94.8, 100.0)
6 months	NE (NE, NE)	95.7 (91.2, 100.0)
9 months	NE (NE, NE)	95.7 (91.2, 100.0)
12 months	NE (NE, NE)	95.7 (91.2, 100.0)
18 months	NE (NE, NE)	95.7 (91.2, 100.0)
Median Follow-up Time (months)	2.83	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	1 (1.6)	2 (1.6)
Number of Subjects Censored, n (%)	63 (98.4)	122 (98.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.977 (1.238)
95% CI		(0.086, 11.066)
Log-rank p-value		0.988

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (94.3, 100.0)	98.4 (96.2, 100.0)
6 months	NE (NE, NE)	98.4 (96.2, 100.0)
9 months	NE (NE, NE)	98.4 (96.2, 100.0)
12 months	NE (NE, NE)	98.4 (96.2, 100.0)
18 months	NE (NE, NE)	98.4 (96.2, 100.0)
Median Follow-up Time (months)	2.83	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	5 (7.8)	0
Number of Subjects Censored, n (%)	59 (92.2)	124 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.9 (85.2, 98.7)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	14 (21.9)	41 (33.1)
Number of Subjects Censored, n (%)	50 (78.1)	83 (66.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.85, NE)	2.79 (1.45, 4.63)
Median (95% CI)	NE (NE, NE)	NE (5.68, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.1, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.245 (0.317)
95% CI		(0.669, 2.319)
Log-rank p-value		0.423

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.0 (67.8, 88.2)	72.0 (63.9, 80.2)
6 months	NE (NE, NE)	60.4 (49.0, 71.7)
9 months	NE (NE, NE)	52.6 (38.2, 66.9)
12 months	NE (NE, NE)	52.6 (38.2, 66.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	8 (12.5)	21 (16.9)
Number of Subjects Censored, n (%)	56 (87.5)	103 (83.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.63, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.141 (0.427)
95% CI		(0.494, 2.633)
Log-rank p-value		0.745

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.1 (78.7, 95.5)	85.5 (79.1, 91.9)
6 months	NE (NE, NE)	82.1 (74.4, 89.8)
9 months	NE (NE, NE)	75.6 (64.3, 86.8)
12 months	NE (NE, NE)	75.6 (64.3, 86.8)
18 months	NE (NE, NE)	75.6 (64.3, 86.8)
Median Follow-up Time (months)	2.83	3.43

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	0	3 (2.4)
Number of Subjects Censored, n (%)	64 (100.0)	121 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.287

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.3 (95.9, 100.0)
6 months	NE (NE, NE)	98.3 (95.9, 100.0)
9 months	NE (NE, NE)	94.0 (85.5, 100.0)
12 months	NE (NE, NE)	94.0 (85.5, 100.0)
18 months	NE (NE, NE)	94.0 (85.5, 100.0)
Median Follow-up Time (months)	2.83	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	0	4 (3.2)
Number of Subjects Censored, n (%)	64 (100.0)	120 (96.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.150

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.7 (93.5, 99.9)
6 months	NE (NE, NE)	96.7 (93.5, 99.9)
9 months	NE (NE, NE)	96.7 (93.5, 99.9)
12 months	NE (NE, NE)	96.7 (93.5, 99.9)
18 months	NE (NE, NE)	96.7 (93.5, 99.9)
Median Follow-up Time (months)	2.83	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	0	6 (4.8)
Number of Subjects Censored, n (%)	64 (100.0)	118 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.51, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.137

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.7 (93.4, 99.9)
6 months	NE (NE, NE)	95.1 (90.7, 99.5)
9 months	NE (NE, NE)	89.5 (78.1, 100.0)
12 months	NE (NE, NE)	89.5 (78.1, 100.0)
18 months	NE (NE, NE)	89.5 (78.1, 100.0)
Median Follow-up Time (months)	2.83	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	2 (3.1)	4 (3.2)
Number of Subjects Censored, n (%)	62 (96.9)	120 (96.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 5.6*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.852 (0.894)
95% CI		(0.148, 4.908)
Log-rank p-value		0.982

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (92.6, 100.0)	97.6 (94.9, 100.0)
6 months	NE (NE, NE)	95.1 (89.7, 100.0)
9 months	NE (NE, NE)	95.1 (89.7, 100.0)
12 months	NE (NE, NE)	95.1 (89.7, 100.0)
18 months	NE (NE, NE)	95.1 (89.7, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	0	5 (4.0)
Number of Subjects Censored, n (%)	64 (100.0)	119 (96.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.10, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.188

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.5 (94.8, 100.0)
6 months	NE (NE, NE)	94.8 (88.9, 100.0)
9 months	NE (NE, NE)	90.7 (81.0, 100.0)
12 months	NE (NE, NE)	90.7 (81.0, 100.0)
18 months	NE (NE, NE)	90.7 (81.0, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	1 (1.6)	4 (3.2)
Number of Subjects Censored, n (%)	63 (98.4)	120 (96.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.575 (1.130)
95% CI		(0.172, 14.427)
Log-rank p-value		0.664

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (95.2, 100.0)	96.5 (93.1, 99.9)
6 months	NE (NE, NE)	96.5 (93.1, 99.9)
9 months	NE (NE, NE)	96.5 (93.1, 99.9)
12 months	NE (NE, NE)	96.5 (93.1, 99.9)
18 months	NE (NE, NE)	96.5 (93.1, 99.9)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	0	4 (3.2)
Number of Subjects Censored, n (%)	64 (100.0)	120 (96.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.51, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.259

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.4 (96.1, 100.0)
6 months	NE (NE, NE)	97.1 (93.8, 100.0)
9 months	NE (NE, NE)	91.7 (81.0, 100.0)
12 months	NE (NE, NE)	91.7 (81.0, 100.0)
18 months	NE (NE, NE)	91.7 (81.0, 100.0)
Median Follow-up Time (months)	2.83	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	2 (3.1)	1 (0.8)
Number of Subjects Censored, n (%)	62 (96.9)	123 (99.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.233 (1.235)
95% CI		(0.021, 2.618)
Log-rank p-value		0.194

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (92.6, 100.0)	99.2 (97.6, 100.0)
6 months	NE (NE, NE)	99.2 (97.6, 100.0)
9 months	NE (NE, NE)	99.2 (97.6, 100.0)
12 months	NE (NE, NE)	99.2 (97.6, 100.0)
18 months	NE (NE, NE)	99.2 (97.6, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	1 (1.6)	0
Number of Subjects Censored, n (%)	63 (98.4)	124 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.200

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (95.1, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	100.0 (100.0, 100.0)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	11 (17.2)	48 (38.7)
Number of Subjects Censored, n (%)	53 (82.8)	76 (61.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.99, NE)	1.61 (0.92, 2.79)
Median (95% CI)	NE (NE, NE)	16.79 (4.67, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (16.79, NE)
Min, Max	0.6, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.061 (0.340)
95% CI		(1.059, 4.011)
Log-rank p-value		0.033

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.5 (71.3, 91.6)	64.7 (56.1, 73.4)
6 months	NE (NE, NE)	57.2 (46.7, 67.7)
9 months	NE (NE, NE)	52.8 (40.1, 65.6)
12 months	NE (NE, NE)	52.8 (40.1, 65.6)
18 months	NE (NE, NE)	26.4 (0.0, 63.6)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	4 (6.3)	15 (12.1)
Number of Subjects Censored, n (%)	60 (93.8)	109 (87.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.87, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.453 (0.581)
95% CI		(0.466, 4.535)
Log-rank p-value		0.514

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.9 (84.1, 99.7)	90.0 (84.6, 95.4)
6 months	NE (NE, NE)	88.3 (82.1, 94.5)
9 months	NE (NE, NE)	80.8 (69.2, 92.3)
12 months	NE (NE, NE)	80.8 (69.2, 92.3)
18 months	NE (NE, NE)	80.8 (69.2, 92.3)
Median Follow-up Time (months)	2.83	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	2 (3.1)	15 (12.1)
Number of Subjects Censored, n (%)	62 (96.9)	109 (87.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.78, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.893 (0.764)
95% CI		(0.647, 12.933)
Log-rank p-value		0.133

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (92.6, 100.0)	90.2 (84.9, 95.5)
6 months	NE (NE, NE)	84.4 (76.3, 92.6)
9 months	NE (NE, NE)	84.4 (76.3, 92.6)
12 months	NE (NE, NE)	84.4 (76.3, 92.6)
18 months	NE (NE, NE)	84.4 (76.3, 92.6)
Median Follow-up Time (months)	2.83	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	1 (1.6)	13 (10.5)
Number of Subjects Censored, n (%)	63 (98.4)	111 (89.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.374 (1.046)
95% CI		(0.692, 41.707)
Log-rank p-value		0.068

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (95.4, 100.0)	90.8 (85.6, 96.0)
6 months	NE (NE, NE)	87.6 (81.0, 94.2)
9 months	NE (NE, NE)	87.6 (81.0, 94.2)
12 months	NE (NE, NE)	87.6 (81.0, 94.2)
18 months	NE (NE, NE)	87.6 (81.0, 94.2)
Median Follow-up Time (months)	2.83	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	1 (1.6)	6 (4.8)
Number of Subjects Censored, n (%)	63 (98.4)	118 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.416 (1.097)
95% CI		(0.281, 20.748)
Log-rank p-value		0.413

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (95.4, 100.0)	95.8 (92.2, 99.4)
6 months	NE (NE, NE)	94.3 (89.6, 98.9)
9 months	NE (NE, NE)	94.3 (89.6, 98.9)
12 months	NE (NE, NE)	94.3 (89.6, 98.9)
18 months	NE (NE, NE)	94.3 (89.6, 98.9)
Median Follow-up Time (months)	2.83	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	1 (1.6)	7 (5.6)
Number of Subjects Censored, n (%)	63 (98.4)	117 (94.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.51, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.071 (1.081)
95% CI		(0.369, 25.562)
Log-rank p-value		0.257

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (95.3, 100.0)	94.7 (90.6, 98.8)
6 months	NE (NE, NE)	94.7 (90.6, 98.8)
9 months	NE (NE, NE)	89.5 (78.7, 100.0)
12 months	NE (NE, NE)	89.5 (78.7, 100.0)
18 months	NE (NE, NE)	89.5 (78.7, 100.0)
Median Follow-up Time (months)	2.83	3.56

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	3 (4.7)	7 (5.6)
Number of Subjects Censored, n (%)	61 (95.3)	117 (94.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.700 (0.731)
95% CI		(0.167, 2.934)
Log-rank p-value		0.622

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (89.8, 100.0)	95.9 (92.3, 99.4)
6 months	NE (NE, NE)	91.5 (84.6, 98.5)
9 months	NE (NE, NE)	91.5 (84.6, 98.5)
12 months	NE (NE, NE)	91.5 (84.6, 98.5)
18 months	NE (NE, NE)	91.5 (84.6, 98.5)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	0	8 (6.5)
Number of Subjects Censored, n (%)	64 (100.0)	116 (93.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.051

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	92.9 (88.1, 97.7)
6 months	NE (NE, NE)	92.9 (88.1, 97.7)
9 months	NE (NE, NE)	92.9 (88.1, 97.7)
12 months	NE (NE, NE)	92.9 (88.1, 97.7)
18 months	NE (NE, NE)	92.9 (88.1, 97.7)
Median Follow-up Time (months)	2.83	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	1 (1.6)	4 (3.2)
Number of Subjects Censored, n (%)	63 (98.4)	120 (96.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.350 (1.141)
95% CI		(0.144, 12.622)
Log-rank p-value		0.819

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (94.3, 100.0)	97.2 (94.0, 100.0)
6 months	NE (NE, NE)	95.2 (90.2, 100.0)
9 months	NE (NE, NE)	95.2 (90.2, 100.0)
12 months	NE (NE, NE)	95.2 (90.2, 100.0)
18 months	NE (NE, NE)	95.2 (90.2, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	1 (1.6)	1 (0.8)
Number of Subjects Censored, n (%)	63 (98.4)	123 (99.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.364 (1.446)
95% CI		(0.021, 6.199)
Log-rank p-value		0.443

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (95.3, 100.0)	98.8 (96.4, 100.0)
6 months	NE (NE, NE)	98.8 (96.4, 100.0)
9 months	NE (NE, NE)	98.8 (96.4, 100.0)
12 months	NE (NE, NE)	98.8 (96.4, 100.0)
18 months	NE (NE, NE)	98.8 (96.4, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	1 (1.6)	1 (0.8)
Number of Subjects Censored, n (%)	63 (98.4)	123 (99.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.469 (1.415)
95% CI		(0.029, 7.509)
Log-rank p-value		0.584

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (95.3, 100.0)	99.1 (97.4, 100.0)
6 months	NE (NE, NE)	99.1 (97.4, 100.0)
9 months	NE (NE, NE)	99.1 (97.4, 100.0)
12 months	NE (NE, NE)	99.1 (97.4, 100.0)
18 months	NE (NE, NE)	99.1 (97.4, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	12 (18.8)	39 (31.5)
Number of Subjects Censored, n (%)	52 (81.3)	85 (68.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.54, NE)	1.87 (0.85, 7.56)
Median (95% CI)	NE (NE, NE)	NE (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.624 (0.336)
95% CI		(0.842, 3.135)
Log-rank p-value		0.140

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.4 (68.7, 90.0)	72.1 (64.1, 80.1)
6 months	NE (NE, NE)	67.1 (57.9, 76.4)
9 months	NE (NE, NE)	63.4 (52.1, 74.6)
12 months	NE (NE, NE)	50.7 (26.7, 74.7)
18 months	NE (NE, NE)	50.7 (26.7, 74.7)
Median Follow-up Time (months)	2.78	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	3 (4.7)	18 (14.5)
Number of Subjects Censored, n (%)	61 (95.3)	106 (85.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.437 (0.625)
95% CI		(1.010, 11.696)
Log-rank p-value		0.034

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.5 (88.3, 100.0)	85.2 (78.9, 91.5)
6 months	NE (NE, NE)	85.2 (78.9, 91.5)
9 months	NE (NE, NE)	85.2 (78.9, 91.5)
12 months	NE (NE, NE)	85.2 (78.9, 91.5)
18 months	NE (NE, NE)	85.2 (78.9, 91.5)
Median Follow-up Time (months)	2.83	3.45

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	3 (4.7)	10 (8.1)
Number of Subjects Censored, n (%)	61 (95.3)	114 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	14.32 (10.28, NE)
Median (95% CI)	NE (NE, NE)	NE (14.32, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (14.32, NE)
Min, Max	0.3, 5.6*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.203 (0.689)
95% CI		(0.312, 4.644)
Log-rank p-value		0.691

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.3 (90.1, 100.0)	94.2 (90.1, 98.4)
6 months	NE (NE, NE)	92.5 (87.1, 97.8)
9 months	NE (NE, NE)	92.5 (87.1, 97.8)
12 months	NE (NE, NE)	84.8 (69.5, 100.0)
18 months	NE (NE, NE)	56.5 (10.2, 100.0)
Median Follow-up Time (months)	2.83	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	4 (6.3)	7 (5.6)
Number of Subjects Censored, n (%)	60 (93.8)	117 (94.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.680 (0.651)
95% CI		(0.190, 2.435)
Log-rank p-value		0.593

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.7 (87.7, 99.7)	95.0 (91.2, 98.9)
6 months	NE (NE, NE)	95.0 (91.2, 98.9)
9 months	NE (NE, NE)	95.0 (91.2, 98.9)
12 months	NE (NE, NE)	83.2 (61.1, 100.0)
18 months	NE (NE, NE)	83.2 (61.1, 100.0)
Median Follow-up Time (months)	2.83	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	1 (1.6)	2 (1.6)
Number of Subjects Censored, n (%)	63 (98.4)	122 (98.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.648 (1.273)
95% CI		(0.053, 7.857)
Log-rank p-value		0.736

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (95.4, 100.0)	98.3 (95.9, 100.0)
6 months	NE (NE, NE)	98.3 (95.9, 100.0)
9 months	NE (NE, NE)	98.3 (95.9, 100.0)
12 months	NE (NE, NE)	98.3 (95.9, 100.0)
18 months	NE (NE, NE)	98.3 (95.9, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	0	1 (0.8)
Number of Subjects Censored, n (%)	64 (100.0)	123 (99.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	97.8 (93.6, 100.0)
9 months	NE (NE, NE)	97.8 (93.6, 100.0)
12 months	NE (NE, NE)	97.8 (93.6, 100.0)
18 months	NE (NE, NE)	97.8 (93.6, 100.0)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Vascular disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	8 (12.5)	44 (35.5)
Number of Subjects Censored, n (%)	56 (87.5)	80 (64.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.53, NE)	1.05 (0.69, 2.96)
Median (95% CI)	NE (NE, NE)	NE (6.93, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.115 (0.388)
95% CI		(1.455, 6.666)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Vascular disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.5 (77.7, 95.3)	66.8 (58.3, 75.3)
6 months	NE (NE, NE)	62.8 (53.1, 72.5)
9 months	NE (NE, NE)	52.7 (37.5, 67.9)
12 months	NE (NE, NE)	52.7 (37.5, 67.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	5 (7.8)	43 (34.7)
Number of Subjects Censored, n (%)	59 (92.2)	81 (65.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.12 (0.69, 3.71)
Median (95% CI)	NE (NE, NE)	7.39 (6.93, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.629 (0.477)
95% CI		(1.819, 11.785)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.3 (84.0, 98.7)	68.4 (60.0, 76.8)
6 months	NE (NE, NE)	64.4 (54.8, 74.0)
9 months	NE (NE, NE)	49.8 (33.5, 66.2)
12 months	NE (NE, NE)	49.8 (33.5, 66.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	12 (18.8)	34 (27.4)
Number of Subjects Censored, n (%)	52 (81.3)	90 (72.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.64, NE)	4.70 (1.15, 7.66)
Median (95% CI)	NE (NE, NE)	NE (7.66, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.257 (0.345)
95% CI		(0.639, 2.473)
Log-rank p-value		0.560

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.8 (69.5, 90.2)	76.6 (68.9, 84.2)
6 months	NE (NE, NE)	65.6 (54.3, 76.8)
9 months	NE (NE, NE)	60.9 (47.2, 74.6)
12 months	NE (NE, NE)	60.9 (47.2, 74.6)
18 months	NE (NE, NE)	60.9 (47.2, 74.6)
Median Follow-up Time (months)	2.78	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	2 (3.1)	11 (8.9)
Number of Subjects Censored, n (%)	62 (96.9)	113 (91.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.334 (0.783)
95% CI		(0.503, 10.821)
Log-rank p-value		0.297

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.6 (91.9, 100.0)	92.0 (86.9, 97.1)
6 months	NE (NE, NE)	88.4 (81.4, 95.4)
9 months	NE (NE, NE)	88.4 (81.4, 95.4)
12 months	NE (NE, NE)	88.4 (81.4, 95.4)
18 months	NE (NE, NE)	88.4 (81.4, 95.4)
Median Follow-up Time (months)	2.83	3.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	4 (6.3)	12 (9.7)
Number of Subjects Censored, n (%)	60 (93.8)	112 (90.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.457 (0.585)
95% CI		(0.463, 4.588)
Log-rank p-value		0.531

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.6 (87.5, 99.7)	90.9 (85.7, 96.0)
6 months	NE (NE, NE)	89.1 (83.1, 95.2)
9 months	NE (NE, NE)	89.1 (83.1, 95.2)
12 months	NE (NE, NE)	89.1 (83.1, 95.2)
18 months	NE (NE, NE)	89.1 (83.1, 95.2)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	2 (3.1)	8 (6.5)
Number of Subjects Censored, n (%)	62 (96.9)	116 (93.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.982 (0.800)
95% CI		(0.413, 9.502)
Log-rank p-value		0.367

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.7 (92.1, 100.0)	94.2 (90.1, 98.4)
6 months	NE (NE, NE)	91.7 (85.3, 98.1)
9 months	NE (NE, NE)	91.7 (85.3, 98.1)
12 months	NE (NE, NE)	91.7 (85.3, 98.1)
18 months	NE (NE, NE)	91.7 (85.3, 98.1)
Median Follow-up Time (months)	2.83	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	1 (1.6)	1 (0.8)
Number of Subjects Censored, n (%)	63 (98.4)	123 (99.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.412 (1.445)
95% CI		(0.024, 6.992)
Log-rank p-value		0.568

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (95.4, 100.0)	99.1 (97.5, 100.0)
6 months	NE (NE, NE)	99.1 (97.5, 100.0)
9 months	NE (NE, NE)	99.1 (97.5, 100.0)
12 months	NE (NE, NE)	99.1 (97.5, 100.0)
18 months	NE (NE, NE)	99.1 (97.5, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	0	2 (1.6)
Number of Subjects Censored, n (%)	64 (100.0)	122 (98.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.434

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.2 (97.6, 100.0)
6 months	NE (NE, NE)	99.2 (97.6, 100.0)
9 months	NE (NE, NE)	95.5 (88.3, 100.0)
12 months	NE (NE, NE)	95.5 (88.3, 100.0)
18 months	NE (NE, NE)	95.5 (88.3, 100.0)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	0	2 (1.6)
Number of Subjects Censored, n (%)	64 (100.0)	122 (98.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.352

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.4 (96.1, 100.0)
6 months	NE (NE, NE)	98.4 (96.1, 100.0)
9 months	NE (NE, NE)	98.4 (96.1, 100.0)
12 months	NE (NE, NE)	98.4 (96.1, 100.0)
18 months	NE (NE, NE)	98.4 (96.1, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	4 (6.3)	36 (29.0)
Number of Subjects Censored, n (%)	60 (93.8)	88 (71.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.71 (0.95, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.707 (0.530)
95% CI		(1.666, 13.301)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.6 (87.6, 99.7)	72.0 (63.9, 80.0)
6 months	NE (NE, NE)	67.8 (58.1, 77.4)
9 months	NE (NE, NE)	67.8 (58.1, 77.4)
12 months	NE (NE, NE)	67.8 (58.1, 77.4)
18 months	NE (NE, NE)	67.8 (58.1, 77.4)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	0	19 (15.3)
Number of Subjects Censored, n (%)	64 (100.0)	105 (84.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.60, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	86.9 (80.9, 92.9)
6 months	NE (NE, NE)	80.5 (71.3, 89.7)
9 months	NE (NE, NE)	80.5 (71.3, 89.7)
12 months	NE (NE, NE)	80.5 (71.3, 89.7)
18 months	NE (NE, NE)	80.5 (71.3, 89.7)
Median Follow-up Time (months)	2.83	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	0	4 (3.2)
Number of Subjects Censored, n (%)	64 (100.0)	120 (96.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.166

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.8 (93.6, 99.9)
6 months	NE (NE, NE)	96.8 (93.6, 99.9)
9 months	NE (NE, NE)	96.8 (93.6, 99.9)
12 months	NE (NE, NE)	96.8 (93.6, 99.9)
18 months	NE (NE, NE)	96.8 (93.6, 99.9)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	0	3 (2.4)
Number of Subjects Censored, n (%)	64 (100.0)	121 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.174

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.6 (94.8, 100.0)
6 months	NE (NE, NE)	97.6 (94.8, 100.0)
9 months	NE (NE, NE)	97.6 (94.8, 100.0)
12 months	NE (NE, NE)	97.6 (94.8, 100.0)
18 months	NE (NE, NE)	97.6 (94.8, 100.0)
Median Follow-up Time (months)	2.83	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	8 (12.5)	33 (26.6)
Number of Subjects Censored, n (%)	56 (87.5)	91 (73.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.25 (1.25, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.014 (0.398)
95% CI		(0.923, 4.397)
Log-rank p-value		0.093

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.4 (79.2, 95.6)	76.1 (68.4, 83.7)
6 months	NE (NE, NE)	69.0 (59.4, 78.7)
9 months	NE (NE, NE)	69.0 (59.4, 78.7)
12 months	NE (NE, NE)	69.0 (59.4, 78.7)
18 months	NE (NE, NE)	69.0 (59.4, 78.7)
Median Follow-up Time (months)	2.83	3.14

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	3 (4.7)	11 (8.9)
Number of Subjects Censored, n (%)	61 (95.3)	113 (91.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.985 (0.656)
95% CI		(0.548, 7.183)
Log-rank p-value		0.312

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (89.7, 100.0)	91.7 (86.8, 96.6)
6 months	NE (NE, NE)	89.8 (83.7, 95.9)
9 months	NE (NE, NE)	89.8 (83.7, 95.9)
12 months	NE (NE, NE)	89.8 (83.7, 95.9)
18 months	NE (NE, NE)	89.8 (83.7, 95.9)
Median Follow-up Time (months)	2.83	3.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	2 (3.1)	6 (4.8)
Number of Subjects Censored, n (%)	62 (96.9)	118 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.219 (0.828)
95% CI		(0.240, 6.180)
Log-rank p-value		0.800

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (92.6, 100.0)	95.0 (91.0, 98.9)
6 months	NE (NE, NE)	95.0 (91.0, 98.9)
9 months	NE (NE, NE)	95.0 (91.0, 98.9)
12 months	NE (NE, NE)	95.0 (91.0, 98.9)
18 months	NE (NE, NE)	95.0 (91.0, 98.9)
Median Follow-up Time (months)	2.83	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	1 (1.6)	4 (3.2)
Number of Subjects Censored, n (%)	63 (98.4)	120 (96.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.826 (1.127)
95% CI		(0.201, 16.621)
Log-rank p-value		0.553

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (95.1, 100.0)	96.6 (93.4, 99.9)
6 months	NE (NE, NE)	96.6 (93.4, 99.9)
9 months	NE (NE, NE)	96.6 (93.4, 99.9)
12 months	NE (NE, NE)	96.6 (93.4, 99.9)
18 months	NE (NE, NE)	96.6 (93.4, 99.9)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	6 (9.4)	24 (19.4)
Number of Subjects Censored, n (%)	58 (90.6)	100 (80.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	6.93 (2.79, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.811 (0.463)
95% CI		(0.730, 4.491)
Log-rank p-value		0.214

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.4 (83.0, 97.7)	81.3 (74.2, 88.4)
6 months	NE (NE, NE)	79.3 (71.3, 87.2)
9 months	NE (NE, NE)	74.6 (63.0, 86.2)
12 months	NE (NE, NE)	74.6 (63.0, 86.2)
18 months	NE (NE, NE)	74.6 (63.0, 86.2)
Median Follow-up Time (months)	2.83	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	2 (3.1)	19 (15.3)
Number of Subjects Censored, n (%)	62 (96.9)	105 (84.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.93, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.765 (0.747)
95% CI		(1.103, 20.596)
Log-rank p-value		0.024

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (92.6, 100.0)	84.7 (78.1, 91.2)
6 months	NE (NE, NE)	84.7 (78.1, 91.2)
9 months	NE (NE, NE)	80.2 (69.7, 90.7)
12 months	NE (NE, NE)	80.2 (69.7, 90.7)
18 months	NE (NE, NE)	80.2 (69.7, 90.7)
Median Follow-up Time (months)	2.83	3.27

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	2 (3.1)	4 (3.2)
Number of Subjects Censored, n (%)	62 (96.9)	120 (96.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 5.6*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.726 (0.903)
95% CI		(0.124, 4.262)
Log-rank p-value		0.737

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.7 (92.2, 100.0)	96.7 (93.6, 99.9)
6 months	NE (NE, NE)	96.7 (93.6, 99.9)
9 months	NE (NE, NE)	96.7 (93.6, 99.9)
12 months	NE (NE, NE)	96.7 (93.6, 99.9)
18 months	NE (NE, NE)	96.7 (93.6, 99.9)
Median Follow-up Time (months)	2.83	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	6 (9.4)	26 (21.0)
Number of Subjects Censored, n (%)	58 (90.6)	98 (79.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	6.28 (3.58, 17.48)
Median (95% CI)	NE (NE, NE)	17.48 (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.48, NE)
Min, Max	0.0, 5.6*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.519 (0.469)
95% CI		(0.605, 3.811)
Log-rank p-value		0.363

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.1 (85.5, 98.8)	86.5 (80.3, 92.7)
6 months	NE (NE, NE)	76.0 (66.1, 85.8)
9 months	NE (NE, NE)	69.0 (56.1, 81.9)
12 months	NE (NE, NE)	59.1 (38.1, 80.1)
18 months	NE (NE, NE)	29.6 (0.0, 71.8)
Median Follow-up Time (months)	2.83	3.37

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	3 (4.7)	7 (5.6)
Number of Subjects Censored, n (%)	61 (95.3)	117 (94.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.700 (0.756)
95% CI		(0.159, 3.082)
Log-rank p-value		0.690

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (92.6, 100.0)	96.6 (93.4, 99.9)
6 months	NE (NE, NE)	92.3 (85.5, 99.0)
9 months	NE (NE, NE)	89.3 (80.6, 98.0)
12 months	NE (NE, NE)	89.3 (80.6, 98.0)
18 months	NE (NE, NE)	89.3 (80.6, 98.0)
Median Follow-up Time (months)	2.83	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	1 (1.6)	5 (4.0)
Number of Subjects Censored, n (%)	63 (98.4)	119 (96.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.56, NE)
Median (95% CI)	NE (NE, NE)	NE (11.56, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.094 (1.161)
95% CI		(0.113, 10.638)
Log-rank p-value		0.962

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (95.3, 100.0)	98.3 (95.9, 100.0)
6 months	NE (NE, NE)	95.4 (90.8, 100.0)
9 months	NE (NE, NE)	95.4 (90.8, 100.0)
12 months	NE (NE, NE)	83.5 (61.2, 100.0)
18 months	NE (NE, NE)	83.5 (61.2, 100.0)
Median Follow-up Time (months)	2.83	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	8 (12.5)	17 (13.7)
Number of Subjects Censored, n (%)	56 (87.5)	107 (86.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.41, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 5.6*	0.0, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.955 (0.441)
95% CI		(0.402, 2.266)
Log-rank p-value		0.922

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.3 (79.1, 95.5)	88.1 (82.2, 94.0)
6 months	NE (NE, NE)	85.0 (77.9, 92.2)
9 months	NE (NE, NE)	81.9 (72.7, 91.0)
12 months	NE (NE, NE)	81.9 (72.7, 91.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	5 (7.8)	10 (8.1)
Number of Subjects Censored, n (%)	59 (92.2)	114 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	17.74 (17.74, NE)
Median (95% CI)	NE (NE, NE)	17.74 (17.74, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.74, NE)
Min, Max	0.7, 5.6*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.767 (0.582)
95% CI		(0.245, 2.400)
Log-rank p-value		0.647

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.0 (85.3, 98.7)	95.0 (91.1, 98.9)
6 months	NE (NE, NE)	92.1 (86.6, 97.6)
9 months	NE (NE, NE)	89.5 (82.1, 96.8)
12 months	NE (NE, NE)	89.5 (82.1, 96.8)
18 months	NE (NE, NE)	44.7 (0.0, 100.0)
Median Follow-up Time (months)	2.83	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	1 (1.6)	10 (8.1)
Number of Subjects Censored, n (%)	63 (98.4)	114 (91.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 5.6*	0.7, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.879 (1.053)
95% CI		(0.619, 38.429)
Log-rank p-value		0.094

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (95.4, 100.0)	91.5 (86.3, 96.6)
6 months	NE (NE, NE)	91.5 (86.3, 96.6)
9 months	NE (NE, NE)	91.5 (86.3, 96.6)
12 months	NE (NE, NE)	91.5 (86.3, 96.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Endocrine disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	0	29 (23.4)
Number of Subjects Censored, n (%)	64 (100.0)	95 (76.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.84 (2.63, NE)
Median (95% CI)	NE (NE, NE)	NE (9.33, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.7, 12.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Endocrine disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	81.2 (74.1, 88.3)
6 months	NE (NE, NE)	72.3 (62.5, 82.1)
9 months	NE (NE, NE)	68.0 (55.8, 80.3)
12 months	NE (NE, NE)	61.2 (44.4, 78.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	0	29 (23.4)
Number of Subjects Censored, n (%)	64 (100.0)	95 (76.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.84 (2.63, NE)
Median (95% CI)	NE (NE, NE)	NE (9.33, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.7, 12.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	81.2 (74.1, 88.3)
6 months	NE (NE, NE)	72.3 (62.5, 82.1)
9 months	NE (NE, NE)	68.0 (55.8, 80.3)
12 months	NE (NE, NE)	61.2 (44.4, 78.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	6 (9.4)	17 (13.7)
Number of Subjects Censored, n (%)	58 (90.6)	107 (86.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.63, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.093 (0.488)
95% CI		(0.420, 2.844)
Log-rank p-value		0.981

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.7 (81.9, 97.6)	88.8 (83.1, 94.6)
6 months	NE (NE, NE)	82.5 (74.4, 90.6)
9 months	NE (NE, NE)	82.5 (74.4, 90.6)
12 months	NE (NE, NE)	82.5 (74.4, 90.6)
18 months	NE (NE, NE)	82.5 (74.4, 90.6)
Median Follow-up Time (months)	2.83	3.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	5 (7.8)	5 (4.0)
Number of Subjects Censored, n (%)	59 (92.2)	119 (96.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.267 (0.673)
95% CI		(0.071, 0.998)
Log-rank p-value		0.019

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.6 (84.6, 98.7)	97.4 (94.5, 100.0)
6 months	NE (NE, NE)	94.2 (88.9, 99.5)
9 months	NE (NE, NE)	94.2 (88.9, 99.5)
12 months	NE (NE, NE)	94.2 (88.9, 99.5)
18 months	NE (NE, NE)	94.2 (88.9, 99.5)
Median Follow-up Time (months)	2.83	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	0	5 (4.0)
Number of Subjects Censored, n (%)	64 (100.0)	119 (96.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.111

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.8 (92.2, 99.4)
6 months	NE (NE, NE)	95.8 (92.2, 99.4)
9 months	NE (NE, NE)	95.8 (92.2, 99.4)
12 months	NE (NE, NE)	95.8 (92.2, 99.4)
18 months	NE (NE, NE)	95.8 (92.2, 99.4)
Median Follow-up Time (months)	2.83	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	1 (1.6)	7 (5.6)
Number of Subjects Censored, n (%)	63 (98.4)	117 (94.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.659 (1.075)
95% CI		(0.445, 30.063)
Log-rank p-value		0.210

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (94.3, 100.0)	94.9 (91.0, 98.9)
6 months	NE (NE, NE)	93.4 (88.5, 98.3)
9 months	NE (NE, NE)	93.4 (88.5, 98.3)
12 months	NE (NE, NE)	93.4 (88.5, 98.3)
18 months	NE (NE, NE)	93.4 (88.5, 98.3)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	3 (4.7)	6 (4.8)
Number of Subjects Censored, n (%)	61 (95.3)	118 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.66, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 5.6*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.519 (0.788)
95% CI		(0.111, 2.430)
Log-rank p-value		0.610

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.3 (90.1, 100.0)	97.4 (94.6, 100.0)
6 months	NE (NE, NE)	95.8 (91.7, 100.0)
9 months	NE (NE, NE)	91.7 (82.7, 100.0)
12 months	NE (NE, NE)	85.6 (71.3, 99.8)
18 months	NE (NE, NE)	85.6 (71.3, 99.8)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	0	2 (1.6)
Number of Subjects Censored, n (%)	64 (100.0)	122 (98.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.66, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.429

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.2 (97.6, 100.0)
6 months	NE (NE, NE)	99.2 (97.6, 100.0)
9 months	NE (NE, NE)	99.2 (97.6, 100.0)
12 months	NE (NE, NE)	92.6 (80.0, 100.0)
18 months	NE (NE, NE)	92.6 (80.0, 100.0)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Number of Subjects with Events, n (%)	0	2 (1.6)
Number of Subjects Censored, n (%)	64 (100.0)	122 (98.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0*, 5.6*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.564

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
<=3

Statistics	Placebo + BSC N=64	Fruquintinib + BSC N=124
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.1 (97.2, 100.0)
6 months	NE (NE, NE)	99.1 (97.2, 100.0)
9 months	NE (NE, NE)	94.8 (86.3, 100.0)
12 months	NE (NE, NE)	94.8 (86.3, 100.0)
18 months	NE (NE, NE)	94.8 (86.3, 100.0)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	99 (59.6)	246 (74.1)
Number of Subjects Censored, n (%)	67 (40.4)	86 (25.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.59 (0.39, 0.69)	0.30 (0.23, 0.46)
Median (95% CI)	1.61 (0.95, 2.56)	0.95 (0.69, 1.35)
75% percentile (95% CI)	NE (4.70, NE)	4.50 (3.65, 6.47)
Min, Max	0.0, 13.0*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.293 (0.120)
95% CI		(1.021, 1.637)
Log-rank p-value		0.042

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	39.4 (31.5, 47.3)	33.0 (27.8, 38.2)
6 months	30.7 (19.4, 42.0)	20.2 (14.9, 25.5)
9 months	30.7 (19.4, 42.0)	13.6 (7.0, 20.2)
12 months	30.7 (19.4, 42.0)	13.6 (7.0, 20.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.38	0.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	40 (24.1)	127 (38.3)
Number of Subjects Censored, n (%)	126 (75.9)	205 (61.7)
Time to first TEAE (months)		
25% percentile (95% CI)	3.22 (0.76, NE)	0.95 (0.69, 1.54)
Median (95% CI)	NE (NE, NE)	NE (8.41, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.523 (0.182)
95% CI		(1.065, 2.178)
Log-rank p-value		0.023

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.4 (68.4, 82.4)	63.8 (58.5, 69.1)
6 months	68.1 (56.1, 80.1)	59.4 (53.6, 65.1)
9 months	68.1 (56.1, 80.1)	55.5 (47.7, 63.4)
12 months	68.1 (56.1, 80.1)	55.5 (47.7, 63.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.35	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	26 (15.7)	69 (20.8)
Number of Subjects Censored, n (%)	140 (84.3)	263 (79.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.65, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.211 (0.232)
95% CI		(0.769, 1.906)
Log-rank p-value		0.442

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.9 (76.8, 89.0)	80.6 (76.3, 85.0)
6 months	82.9 (76.8, 89.0)	77.1 (72.0, 82.1)
9 months	82.9 (76.8, 89.0)	75.5 (69.8, 81.3)
12 months	82.9 (76.8, 89.0)	75.5 (69.8, 81.3)
18 months	NE (NE, NE)	75.5 (69.8, 81.3)
Median Follow-up Time (months)	2.51	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	19 (11.4)	41 (12.3)
Number of Subjects Censored, n (%)	147 (88.6)	291 (87.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.70, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.937 (0.283)
95% CI		(0.538, 1.633)
Log-rank p-value		0.684

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.1 (82.8, 93.3)	89.7 (86.3, 93.0)
6 months	82.9 (71.9, 93.9)	86.1 (81.9, 90.4)
9 months	82.9 (71.9, 93.9)	84.2 (79.2, 89.2)
12 months	82.9 (71.9, 93.9)	84.2 (79.2, 89.2)
18 months	NE (NE, NE)	84.2 (79.2, 89.2)
Median Follow-up Time (months)	2.78	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	5 (3.0)	45 (13.6)
Number of Subjects Censored, n (%)	161 (97.0)	287 (86.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.087 (0.472)
95% CI		(1.619, 10.316)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.6 (93.7, 99.5)	87.3 (83.7, 90.9)
6 months	96.6 (93.7, 99.5)	85.6 (81.5, 89.6)
9 months	96.6 (93.7, 99.5)	84.2 (79.4, 89.0)
12 months	96.6 (93.7, 99.5)	84.2 (79.4, 89.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.37

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	22 (13.3)	18 (5.4)
Number of Subjects Censored, n (%)	144 (86.7)	314 (94.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.291 (0.326)
95% CI		(0.154, 0.552)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.7 (79.9, 91.5)	96.4 (94.2, 98.5)
6 months	83.1 (75.6, 90.6)	92.6 (89.0, 96.3)
9 months	83.1 (75.6, 90.6)	92.6 (89.0, 96.3)
12 months	83.1 (75.6, 90.6)	92.6 (89.0, 96.3)
18 months	NE (NE, NE)	82.3 (63.0, 100.0)
Median Follow-up Time (months)	2.81	4.07

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	13 (7.8)	17 (5.1)
Number of Subjects Censored, n (%)	153 (92.2)	315 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.574 (0.373)
95% CI		(0.276, 1.193)
Log-rank p-value		0.128

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.9 (87.7, 96.1)	95.0 (92.6, 97.4)
6 months	91.9 (87.7, 96.1)	95.0 (92.6, 97.4)
9 months	91.9 (87.7, 96.1)	91.8 (85.3, 98.3)
12 months	91.9 (87.7, 96.1)	91.8 (85.3, 98.3)
18 months	NE (NE, NE)	91.8 (85.3, 98.3)
Median Follow-up Time (months)	2.79	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	4 (2.4)	13 (3.9)
Number of Subjects Censored, n (%)	162 (97.6)	319 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.127 (0.586)
95% CI		(0.357, 3.554)
Log-rank p-value		0.925

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (95.2, 99.9)	97.5 (95.7, 99.2)
6 months	97.5 (95.2, 99.9)	95.2 (92.3, 98.0)
9 months	97.5 (95.2, 99.9)	95.2 (92.3, 98.0)
12 months	97.5 (95.2, 99.9)	90.8 (82.1, 99.6)
18 months	NE (NE, NE)	90.8 (82.1, 99.6)
Median Follow-up Time (months)	2.83	4.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	3 (1.8)	8 (2.4)
Number of Subjects Censored, n (%)	163 (98.2)	324 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.044 (0.683)
95% CI		(0.274, 3.984)
Log-rank p-value		0.958

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (94.8, 100.0)	97.7 (96.0, 99.4)
6 months	97.6 (94.8, 100.0)	97.1 (95.0, 99.1)
9 months	97.6 (94.8, 100.0)	97.1 (95.0, 99.1)
12 months	97.6 (94.8, 100.0)	97.1 (95.0, 99.1)
18 months	NE (NE, NE)	97.1 (95.0, 99.1)
Median Follow-up Time (months)	2.83	4.01

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	2 (1.2)	9 (2.7)
Number of Subjects Censored, n (%)	164 (98.8)	323 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.816 (0.792)
95% CI		(0.384, 8.586)
Log-rank p-value		0.436

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (97.1, 100.0)	97.9 (96.3, 99.4)
6 months	98.8 (97.1, 100.0)	96.3 (93.7, 99.0)
9 months	98.8 (97.1, 100.0)	96.3 (93.7, 99.0)
12 months	98.8 (97.1, 100.0)	96.3 (93.7, 99.0)
18 months	NE (NE, NE)	96.3 (93.7, 99.0)
Median Follow-up Time (months)	2.83	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	96 (57.8)	227 (68.4)
Number of Subjects Censored, n (%)	70 (42.2)	105 (31.6)
Time to first TEAE (months)		
25% percentile (95% CI)	0.62 (0.39, 0.69)	0.46 (0.33, 0.66)
Median (95% CI)	1.61 (1.28, 2.79)	1.38 (0.95, 1.87)
75% percentile (95% CI)	5.36 (3.75, NE)	5.95 (4.50, NE)
Min, Max	0.0, 6.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.066 (0.123)
95% CI		(0.837, 1.358)
Log-rank p-value		0.635

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	39.6 (31.0, 48.3)	37.1 (31.7, 42.5)
6 months	9.3 (0.0, 24.9)	24.2 (18.3, 30.1)
9 months	NE (NE, NE)	21.7 (15.4, 27.9)
12 months	NE (NE, NE)	18.1 (9.8, 26.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.31	1.31

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	17 (10.2)	86 (25.9)
Number of Subjects Censored, n (%)	149 (89.8)	246 (74.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.71 (1.87, 6.70)
Median (95% CI)	NE (NE, NE)	NE (10.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.299 (0.267)
95% CI		(1.362, 3.881)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.2 (84.4, 94.1)	76.6 (71.9, 81.3)
6 months	89.2 (84.4, 94.1)	70.7 (64.8, 76.7)
9 months	89.2 (84.4, 94.1)	68.5 (61.9, 75.0)
12 months	89.2 (84.4, 94.1)	59.9 (43.2, 76.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.64	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	30 (18.1)	62 (18.7)
Number of Subjects Censored, n (%)	136 (81.9)	270 (81.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.79, NE)	8.31 (5.29, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.807 (0.226)
95% CI		(0.518, 1.256)
Log-rank p-value		0.355

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.5 (75.3, 87.7)	82.9 (78.6, 87.2)
6 months	77.2 (67.1, 87.3)	77.8 (72.3, 83.3)
9 months	77.2 (67.1, 87.3)	73.8 (66.8, 80.8)
12 months	77.2 (67.1, 87.3)	73.8 (66.8, 80.8)
18 months	NE (NE, NE)	73.8 (66.8, 80.8)
Median Follow-up Time (months)	2.56	3.20

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	25 (15.1)	58 (17.5)
Number of Subjects Censored, n (%)	141 (84.9)	274 (82.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.92, NE)	10.12 (5.19, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.924 (0.244)
95% CI		(0.573, 1.490)
Log-rank p-value		0.901

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.8 (76.1, 89.6)	84.6 (80.5, 88.7)
6 months	78.9 (69.0, 88.8)	80.4 (75.5, 85.4)
9 months	78.9 (69.0, 88.8)	76.7 (70.2, 83.1)
12 months	78.9 (69.0, 88.8)	71.9 (61.0, 82.8)
18 months	NE (NE, NE)	71.9 (61.0, 82.8)
Median Follow-up Time (months)	2.73	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	18 (10.8)	60 (18.1)
Number of Subjects Censored, n (%)	148 (89.2)	272 (81.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	9.33 (4.21, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.306 (0.273)
95% CI		(0.765, 2.228)
Log-rank p-value		0.334

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.4 (81.1, 93.7)	84.5 (80.4, 88.5)
6 months	85.2 (77.7, 92.7)	79.2 (74.1, 84.4)
9 months	85.2 (77.7, 92.7)	76.4 (70.2, 82.7)
12 months	85.2 (77.7, 92.7)	73.0 (64.0, 81.9)
18 months	NE (NE, NE)	73.0 (64.0, 81.9)
Median Follow-up Time (months)	2.71	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	17 (10.2)	53 (16.0)
Number of Subjects Censored, n (%)	149 (89.8)	279 (84.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.36, NE)	18.04 (6.21, NE)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.1, 13.0*	0.0, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.213 (0.284)
95% CI		(0.696, 2.115)
Log-rank p-value		0.480

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.9 (85.0, 94.8)	86.9 (83.1, 90.7)
6 months	81.9 (69.7, 94.1)	81.4 (76.2, 86.6)
9 months	81.9 (69.7, 94.1)	79.4 (73.7, 85.2)
12 months	81.9 (69.7, 94.1)	75.5 (66.1, 84.8)
18 months	NE (NE, NE)	75.5 (66.1, 84.8)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	7 (4.2)	55 (16.6)
Number of Subjects Censored, n (%)	159 (95.8)	277 (83.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.98, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.884 (0.403)
95% CI		(1.764, 8.551)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.3 (91.9, 98.7)	84.6 (80.6, 88.5)
6 months	95.3 (91.9, 98.7)	82.0 (77.5, 86.6)
9 months	95.3 (91.9, 98.7)	80.3 (74.8, 85.9)
12 months	95.3 (91.9, 98.7)	80.3 (74.8, 85.9)
18 months	NE (NE, NE)	80.3 (74.8, 85.9)
Median Follow-up Time (months)	2.79	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	6 (3.6)	23 (6.9)
Number of Subjects Censored, n (%)	160 (96.4)	309 (93.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.488 (0.466)
95% CI		(0.597, 3.711)
Log-rank p-value		0.480

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.7 (93.9, 99.6)	94.6 (92.1, 97.1)
6 months	89.8 (76.5, 100.0)	90.9 (87.0, 94.7)
9 months	NE (NE, NE)	90.9 (87.0, 94.7)
12 months	NE (NE, NE)	90.9 (87.0, 94.7)
18 months	NE (NE, NE)	90.9 (87.0, 94.7)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	3 (1.8)	12 (3.6)
Number of Subjects Censored, n (%)	163 (98.2)	320 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.657 (0.654)
95% CI		(0.460, 5.970)
Log-rank p-value		0.460

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (95.8, 100.0)	97.0 (95.1, 98.8)
6 months	98.0 (95.8, 100.0)	96.1 (93.6, 98.6)
9 months	98.0 (95.8, 100.0)	94.4 (90.3, 98.5)
12 months	98.0 (95.8, 100.0)	94.4 (90.3, 98.5)
18 months	NE (NE, NE)	94.4 (90.3, 98.5)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	3 (1.8)	9 (2.7)
Number of Subjects Censored, n (%)	163 (98.2)	323 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.355 (0.668)
95% CI		(0.366, 5.020)
Log-rank p-value		0.547

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (95.9, 100.0)	97.1 (95.2, 99.0)
6 months	98.1 (95.9, 100.0)	97.1 (95.2, 99.0)
9 months	98.1 (95.9, 100.0)	97.1 (95.2, 99.0)
12 months	98.1 (95.9, 100.0)	97.1 (95.2, 99.0)
18 months	NE (NE, NE)	97.1 (95.2, 99.0)
Median Follow-up Time (months)	2.81	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	6 (3.6)	3 (0.9)
Number of Subjects Censored, n (%)	160 (96.4)	329 (99.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.182 (0.726)
95% CI		(0.044, 0.756)
Log-rank p-value		0.009

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.0 (92.8, 99.1)	99.4 (98.5, 100.0)
6 months	96.0 (92.8, 99.1)	98.4 (96.4, 100.0)
9 months	96.0 (92.8, 99.1)	98.4 (96.4, 100.0)
12 months	96.0 (92.8, 99.1)	98.4 (96.4, 100.0)
18 months	NE (NE, NE)	98.4 (96.4, 100.0)
Median Follow-up Time (months)	2.79	3.96

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	0	13 (3.9)
Number of Subjects Censored, n (%)	166 (100.0)	319 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.015

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.1 (94.0, 98.3)
6 months	100.0 (100.0, 100.0)	96.1 (94.0, 98.3)
9 months	100.0 (100.0, 100.0)	94.2 (89.9, 98.5)
12 months	100.0 (100.0, 100.0)	94.2 (89.9, 98.5)
18 months	NE (NE, NE)	94.2 (89.9, 98.5)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	49 (29.5)	155 (46.7)
Number of Subjects Censored, n (%)	117 (70.5)	177 (53.3)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.76, 4.27)	0.95 (0.72, 1.54)
Median (95% CI)	10.18 (NE, NE)	6.01 (3.09, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.0, 10.2	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.457 (0.165)
95% CI		(1.054, 2.014)
Log-rank p-value		0.030

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	70.4 (63.1, 77.7)	55.8 (50.2, 61.3)
6 months	64.3 (53.7, 75.0)	50.1 (44.0, 56.1)
9 months	64.3 (53.7, 75.0)	46.6 (40.1, 53.1)
12 months	0.0 (NE, NE)	42.4 (32.5, 52.3)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.33	2.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	32 (19.3)	103 (31.0)
Number of Subjects Censored, n (%)	134 (80.7)	229 (69.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.87, NE)	1.94 (1.45, 2.99)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.468 (0.204)
95% CI		(0.985, 2.188)
Log-rank p-value		0.078

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.0 (73.6, 86.4)	69.9 (64.8, 75.1)
6 months	76.4 (67.1, 85.6)	66.0 (60.3, 71.7)
9 months	76.4 (67.1, 85.6)	65.0 (59.1, 70.9)
12 months	76.4 (67.1, 85.6)	61.6 (53.0, 70.2)
18 months	NE (NE, NE)	61.6 (53.0, 70.2)
Median Follow-up Time (months)	2.58	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	4 (2.4)	25 (7.5)
Number of Subjects Censored, n (%)	162 (97.6)	307 (92.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.697 (0.541)
95% CI		(0.935, 7.779)
Log-rank p-value		0.042

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (95.2, 99.9)	92.3 (89.3, 95.4)
6 months	97.6 (95.2, 99.9)	91.2 (87.8, 94.6)
9 months	97.6 (95.2, 99.9)	91.2 (87.8, 94.6)
12 months	97.6 (95.2, 99.9)	91.2 (87.8, 94.6)
18 months	NE (NE, NE)	91.2 (87.8, 94.6)
Median Follow-up Time (months)	2.81	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	5 (3.0)	16 (4.8)
Number of Subjects Censored, n (%)	161 (97.0)	316 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.052 (0.527)
95% CI		(0.374, 2.955)
Log-rank p-value		0.812

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (95.1, 99.9)	96.4 (94.3, 98.5)
6 months	95.1 (90.0, 100.0)	93.7 (90.3, 97.0)
9 months	95.1 (90.0, 100.0)	92.1 (87.6, 96.6)
12 months	95.1 (90.0, 100.0)	92.1 (87.6, 96.6)
18 months	NE (NE, NE)	92.1 (87.6, 96.6)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	4 (2.4)	8 (2.4)
Number of Subjects Censored, n (%)	162 (97.6)	324 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.956 (0.616)
95% CI		(0.286, 3.198)
Log-rank p-value		0.856

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (94.6, 99.9)	97.4 (95.6, 99.2)
6 months	97.3 (94.6, 99.9)	97.4 (95.6, 99.2)
9 months	97.3 (94.6, 99.9)	97.4 (95.6, 99.2)
12 months	97.3 (94.6, 99.9)	97.4 (95.6, 99.2)
18 months	NE (NE, NE)	97.4 (95.6, 99.2)
Median Follow-up Time (months)	2.79	3.96

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	1 (0.6)	11 (3.3)
Number of Subjects Censored, n (%)	165 (99.4)	321 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.687 (1.051)
95% CI		(0.597, 36.805)
Log-rank p-value		0.116

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	96.7 (94.6, 98.7)
6 months	99.4 (98.2, 100.0)	96.7 (94.6, 98.7)
9 months	99.4 (98.2, 100.0)	95.0 (91.3, 98.8)
12 months	99.4 (98.2, 100.0)	95.0 (91.3, 98.8)
18 months	NE (NE, NE)	95.0 (91.3, 98.8)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	0	13 (3.9)
Number of Subjects Censored, n (%)	166 (100.0)	319 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.020

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.5 (94.5, 98.5)
6 months	100.0 (100.0, 100.0)	95.3 (92.7, 97.9)
9 months	100.0 (100.0, 100.0)	95.3 (92.7, 97.9)
12 months	100.0 (100.0, 100.0)	95.3 (92.7, 97.9)
18 months	NE (NE, NE)	95.3 (92.7, 97.9)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	2 (1.2)	9 (2.7)
Number of Subjects Censored, n (%)	164 (98.8)	323 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.837 (0.789)
95% CI		(0.391, 8.625)
Log-rank p-value		0.448

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (95.6, 100.0)	97.4 (95.7, 99.2)
6 months	98.2 (95.6, 100.0)	97.4 (95.7, 99.2)
9 months	98.2 (95.6, 100.0)	96.4 (93.7, 99.1)
12 months	98.2 (95.6, 100.0)	96.4 (93.7, 99.1)
18 months	NE (NE, NE)	96.4 (93.7, 99.1)
Median Follow-up Time (months)	2.81	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	2 (1.2)	9 (2.7)
Number of Subjects Censored, n (%)	164 (98.8)	323 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.675 (0.792)
95% CI		(0.355, 7.916)
Log-rank p-value		0.520

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (97.1, 100.0)	97.7 (96.1, 99.4)
6 months	98.8 (97.1, 100.0)	96.8 (94.4, 99.2)
9 months	98.8 (97.1, 100.0)	95.8 (92.8, 98.9)
12 months	98.8 (97.1, 100.0)	95.8 (92.8, 98.9)
18 months	NE (NE, NE)	95.8 (92.8, 98.9)
Median Follow-up Time (months)	2.81	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	1 (0.6)	10 (3.0)
Number of Subjects Censored, n (%)	165 (99.4)	322 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Median (95% CI)	10.18 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 10.2	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.698 (1.057)
95% CI		(0.592, 37.299)
Log-rank p-value		0.111

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.8 (94.8, 98.8)
6 months	100.0 (100.0, 100.0)	96.8 (94.8, 98.8)
9 months	100.0 (100.0, 100.0)	96.8 (94.8, 98.8)
12 months	0.0 (NE, NE)	96.8 (94.8, 98.8)
18 months	0.0 (NE, NE)	96.8 (94.8, 98.8)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	0	11 (3.3)
Number of Subjects Censored, n (%)	166 (100.0)	321 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.054

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.2 (96.7, 99.8)
6 months	100.0 (100.0, 100.0)	94.1 (90.5, 97.7)
9 months	100.0 (100.0, 100.0)	94.1 (90.5, 97.7)
12 months	100.0 (100.0, 100.0)	94.1 (90.5, 97.7)
18 months	NE (NE, NE)	94.1 (90.5, 97.7)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	52 (31.3)	138 (41.6)
Number of Subjects Censored, n (%)	114 (68.7)	194 (58.4)
Time to first TEAE (months)		
25% percentile (95% CI)	1.61 (0.95, 3.55)	1.58 (0.95, 1.81)
Median (95% CI)	NE (5.59, NE)	6.67 (5.68, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.145 (0.166)
95% CI		(0.828, 1.584)
Log-rank p-value		0.461

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	69.2 (61.8, 76.5)	62.4 (57.0, 67.8)
6 months	50.3 (31.2, 69.3)	55.2 (48.9, 61.5)
9 months	NE (NE, NE)	47.4 (39.9, 54.8)
12 months	NE (NE, NE)	47.4 (39.9, 54.8)
18 months	NE (NE, NE)	47.4 (39.9, 54.8)
Median Follow-up Time (months)	2.43	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	17 (10.2)	41 (12.3)
Number of Subjects Censored, n (%)	149 (89.8)	291 (87.7)
Time to first TEAE (months)		
25% percentile (95% CI)	5.82 (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.82, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.970 (0.295)
95% CI		(0.544, 1.730)
Log-rank p-value		0.802

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (83.6, 94.3)	89.0 (85.4, 92.5)
6 months	72.3 (50.2, 94.4)	84.7 (79.9, 89.5)
9 months	NE (NE, NE)	83.7 (78.6, 88.8)
12 months	NE (NE, NE)	83.7 (78.6, 88.8)
18 months	NE (NE, NE)	83.7 (78.6, 88.8)
Median Follow-up Time (months)	2.73	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	9 (5.4)	33 (9.9)
Number of Subjects Censored, n (%)	157 (94.6)	299 (90.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.507 (0.388)
95% CI		(0.704, 3.226)
Log-rank p-value		0.380

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (91.5, 98.4)	91.0 (87.7, 94.3)
6 months	88.2 (75.0, 100.0)	89.1 (85.2, 93.0)
9 months	NE (NE, NE)	85.4 (79.8, 91.0)
12 months	NE (NE, NE)	85.4 (79.8, 91.0)
18 months	NE (NE, NE)	85.4 (79.8, 91.0)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	8 (4.8)	34 (10.2)
Number of Subjects Censored, n (%)	158 (95.2)	298 (89.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.655 (0.404)
95% CI		(0.750, 3.652)
Log-rank p-value		0.236

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (92.5, 98.8)	91.6 (88.5, 94.7)
6 months	88.8 (75.6, 100.0)	89.0 (85.0, 93.0)
9 months	NE (NE, NE)	84.3 (78.4, 90.2)
12 months	NE (NE, NE)	84.3 (78.4, 90.2)
18 months	NE (NE, NE)	84.3 (78.4, 90.2)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	10 (6.0)	30 (9.0)
Number of Subjects Censored, n (%)	156 (94.0)	302 (91.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.113 (0.371)
95% CI		(0.538, 2.306)
Log-rank p-value		0.820

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.8 (90.1, 97.5)	92.9 (90.1, 95.8)
6 months	93.8 (90.1, 97.5)	89.4 (85.5, 93.3)
9 months	93.8 (90.1, 97.5)	86.8 (81.5, 92.0)
12 months	93.8 (90.1, 97.5)	86.8 (81.5, 92.0)
18 months	NE (NE, NE)	86.8 (81.5, 92.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	2 (1.2)	25 (7.5)
Number of Subjects Censored, n (%)	164 (98.8)	307 (92.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.195 (0.740)
95% CI		(1.218, 22.153)
Log-rank p-value		0.018

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.4, 100.0)	93.2 (90.4, 96.0)
6 months	96.1 (90.1, 100.0)	91.6 (88.0, 95.2)
9 months	96.1 (90.1, 100.0)	89.6 (85.2, 94.0)
12 months	96.1 (90.1, 100.0)	89.6 (85.2, 94.0)
18 months	NE (NE, NE)	89.6 (85.2, 94.0)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	7 (4.2)	17 (5.1)
Number of Subjects Censored, n (%)	159 (95.8)	315 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.992 (0.456)
95% CI		(0.406, 2.423)
Log-rank p-value		0.942

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (91.4, 98.7)	95.2 (92.8, 97.6)
6 months	95.1 (91.4, 98.7)	94.4 (91.6, 97.2)
9 months	95.1 (91.4, 98.7)	93.4 (90.0, 96.8)
12 months	95.1 (91.4, 98.7)	93.4 (90.0, 96.8)
18 months	NE (NE, NE)	93.4 (90.0, 96.8)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	2 (1.2)	19 (5.7)
Number of Subjects Censored, n (%)	164 (98.8)	313 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	7.43 (7.43, NE)	NE (NE, NE)
Median (95% CI)	7.43 (7.43, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (7.43, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.014 (0.749)
95% CI		(0.925, 17.409)
Log-rank p-value		0.053

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	95.0 (92.6, 97.4)
6 months	99.4 (98.2, 100.0)	93.1 (89.9, 96.3)
9 months	NE (NE, NE)	93.1 (89.9, 96.3)
12 months	NE (NE, NE)	93.1 (89.9, 96.3)
18 months	NE (NE, NE)	93.1 (89.9, 96.3)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	4 (2.4)	16 (4.8)
Number of Subjects Censored, n (%)	162 (97.6)	316 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.443 (0.566)
95% CI		(0.476, 4.379)
Log-rank p-value		0.528

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.9 (95.5, 100.0)	95.8 (93.5, 98.0)
6 months	95.0 (89.0, 100.0)	94.4 (91.5, 97.4)
9 months	95.0 (89.0, 100.0)	93.4 (90.0, 96.9)
12 months	95.0 (89.0, 100.0)	93.4 (90.0, 96.9)
18 months	NE (NE, NE)	93.4 (90.0, 96.9)
Median Follow-up Time (months)	2.79	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	0	12 (3.6)
Number of Subjects Censored, n (%)	166 (100.0)	320 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.031

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.7 (94.7, 98.7)
6 months	100.0 (100.0, 100.0)	96.1 (93.7, 98.4)
9 months	100.0 (100.0, 100.0)	94.7 (91.1, 98.2)
12 months	100.0 (100.0, 100.0)	94.7 (91.1, 98.2)
18 months	NE (NE, NE)	94.7 (91.1, 98.2)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	1 (0.6)	10 (3.0)
Number of Subjects Censored, n (%)	165 (99.4)	322 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.116 (1.054)
95% CI		(0.522, 32.478)
Log-rank p-value		0.145

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.1, 100.0)	97.0 (95.1, 99.0)
6 months	99.4 (98.1, 100.0)	97.0 (95.1, 99.0)
9 months	99.4 (98.1, 100.0)	95.7 (92.4, 98.9)
12 months	99.4 (98.1, 100.0)	95.7 (92.4, 98.9)
18 months	NE (NE, NE)	95.7 (92.4, 98.9)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	45 (27.1)	136 (41.0)
Number of Subjects Censored, n (%)	121 (72.9)	196 (59.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.84 (0.95, NE)	0.69 (0.69, 0.95)
Median (95% CI)	NE (NE, NE)	9.69 (6.34, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.466 (0.174)
95% CI		(1.043, 2.060)
Log-rank p-value		0.032

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.1 (63.9, 78.4)	62.6 (57.3, 67.9)
6 months	71.1 (63.9, 78.4)	56.8 (50.7, 62.8)
9 months	71.1 (63.9, 78.4)	53.8 (47.1, 60.4)
12 months	71.1 (63.9, 78.4)	46.7 (35.8, 57.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.99	2.51

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	9 (5.4)	56 (16.9)
Number of Subjects Censored, n (%)	157 (94.6)	276 (83.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.247 (0.361)
95% CI		(1.600, 6.587)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.3 (90.6, 97.9)	83.2 (79.1, 87.3)
6 months	94.3 (90.6, 97.9)	82.7 (78.5, 86.8)
9 months	94.3 (90.6, 97.9)	82.7 (78.5, 86.8)
12 months	94.3 (90.6, 97.9)	82.7 (78.5, 86.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	19 (11.4)	33 (9.9)
Number of Subjects Censored, n (%)	147 (88.6)	299 (90.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.691 (0.292)
95% CI		(0.390, 1.225)
Log-rank p-value		0.232

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.8 (82.6, 93.0)	91.7 (88.6, 94.8)
6 months	87.8 (82.6, 93.0)	88.6 (84.6, 92.7)
9 months	87.8 (82.6, 93.0)	86.7 (82.0, 91.4)
12 months	87.8 (82.6, 93.0)	86.7 (82.0, 91.4)
18 months	NE (NE, NE)	86.7 (82.0, 91.4)
Median Follow-up Time (months)	2.78	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	17 (10.2)	31 (9.3)
Number of Subjects Censored, n (%)	149 (89.8)	301 (90.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.815 (0.305)
95% CI		(0.448, 1.482)
Log-rank p-value		0.556

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.8 (83.8, 93.9)	91.2 (88.1, 94.3)
6 months	88.8 (83.8, 93.9)	90.0 (86.5, 93.5)
9 months	88.8 (83.8, 93.9)	89.0 (84.9, 93.0)
12 months	88.8 (83.8, 93.9)	89.0 (84.9, 93.0)
18 months	NE (NE, NE)	89.0 (84.9, 93.0)
Median Follow-up Time (months)	2.58	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	2 (1.2)	16 (4.8)
Number of Subjects Censored, n (%)	164 (98.8)	316 (95.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.766 (0.751)
95% CI		(0.865, 16.397)
Log-rank p-value		0.064

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (97.1, 100.0)	95.0 (92.5, 97.4)
6 months	98.8 (97.1, 100.0)	95.0 (92.5, 97.4)
9 months	98.8 (97.1, 100.0)	95.0 (92.5, 97.4)
12 months	98.8 (97.1, 100.0)	95.0 (92.5, 97.4)
18 months	NE (NE, NE)	95.0 (92.5, 97.4)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	2 (1.2)	9 (2.7)
Number of Subjects Censored, n (%)	164 (98.8)	323 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.768 (0.797)
95% CI		(0.371, 8.433)
Log-rank p-value		0.513

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.7, 100.0)	97.9 (96.3, 99.4)
6 months	98.6 (96.7, 100.0)	97.9 (96.3, 99.4)
9 months	98.6 (96.7, 100.0)	95.4 (91.7, 99.1)
12 months	98.6 (96.7, 100.0)	95.4 (91.7, 99.1)
18 months	NE (NE, NE)	95.4 (91.7, 99.1)
Median Follow-up Time (months)	2.81	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Vascular disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	26 (15.7)	135 (40.7)
Number of Subjects Censored, n (%)	140 (84.3)	197 (59.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.61, NE)	0.92 (0.69, 1.58)
Median (95% CI)	NE (NE, NE)	NE (6.44, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.711 (0.215)
95% CI		(1.779, 4.132)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Vascular disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.8 (77.9, 89.7)	59.9 (54.5, 65.3)
6 months	80.6 (72.2, 88.9)	56.5 (50.5, 62.4)
9 months	NE (NE, NE)	53.7 (46.9, 60.5)
12 months	NE (NE, NE)	53.7 (46.9, 60.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.43	2.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	15 (9.0)	125 (37.7)
Number of Subjects Censored, n (%)	151 (91.0)	207 (62.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.95 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.478 (0.274)
95% CI		(2.618, 7.659)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.2 (85.4, 94.9)	62.4 (57.1, 67.8)
6 months	90.2 (85.4, 94.9)	60.6 (54.9, 66.2)
9 months	NE (NE, NE)	57.8 (51.2, 64.4)
12 months	NE (NE, NE)	57.8 (51.2, 64.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.64	2.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	36 (21.7)	119 (35.8)
Number of Subjects Censored, n (%)	130 (78.3)	213 (64.2)
Time to first TEAE (months)		
25% percentile (95% CI)	3.71 (1.61, NE)	1.58 (0.95, 1.84)
Median (95% CI)	NE (5.59, NE)	NE (8.64, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.538 (0.192)
95% CI		(1.056, 2.240)
Log-rank p-value		0.014

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.5 (71.8, 85.2)	65.2 (60.0, 70.5)
6 months	64.6 (47.3, 81.9)	62.5 (56.7, 68.2)
9 months	NE (NE, NE)	56.8 (48.3, 65.3)
12 months	NE (NE, NE)	52.4 (41.1, 63.8)
18 months	NE (NE, NE)	52.4 (41.1, 63.8)
Median Follow-up Time (months)	2.43	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	15 (9.0)	36 (10.8)
Number of Subjects Censored, n (%)	151 (91.0)	296 (89.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.009 (0.312)
95% CI		(0.548, 1.859)
Log-rank p-value		0.934

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.7 (86.3, 95.2)	90.1 (86.8, 93.4)
6 months	90.7 (86.3, 95.2)	87.6 (83.6, 91.7)
9 months	90.7 (86.3, 95.2)	86.7 (82.3, 91.1)
12 months	90.7 (86.3, 95.2)	86.7 (82.3, 91.1)
18 months	NE (NE, NE)	86.7 (82.3, 91.1)
Median Follow-up Time (months)	2.78	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	6 (3.6)	38 (11.4)
Number of Subjects Censored, n (%)	160 (96.4)	294 (88.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (7.98, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.593 (0.443)
95% CI		(1.087, 6.184)
Log-rank p-value		0.028

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.8 (94.1, 99.6)	90.2 (86.9, 93.5)
6 months	89.9 (76.6, 100.0)	87.2 (82.8, 91.6)
9 months	NE (NE, NE)	82.3 (75.4, 89.2)
12 months	NE (NE, NE)	82.3 (75.4, 89.2)
18 months	NE (NE, NE)	82.3 (75.4, 89.2)
Median Follow-up Time (months)	2.79	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	3 (1.8)	18 (5.4)
Number of Subjects Censored, n (%)	163 (98.2)	314 (94.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.581 (0.627)
95% CI		(0.756, 8.815)
Log-rank p-value		0.087

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	94.6 (92.1, 97.1)
6 months	93.6 (85.6, 100.0)	93.8 (90.9, 96.8)
9 months	93.6 (85.6, 100.0)	93.8 (90.9, 96.8)
12 months	93.6 (85.6, 100.0)	93.8 (90.9, 96.8)
18 months	NE (NE, NE)	93.8 (90.9, 96.8)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	4 (2.4)	13 (3.9)
Number of Subjects Censored, n (%)	162 (97.6)	319 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.439 (0.576)
95% CI		(0.465, 4.450)
Log-rank p-value		0.508

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (95.0, 99.9)	96.2 (94.0, 98.3)
6 months	97.5 (95.0, 99.9)	95.2 (92.4, 98.0)
9 months	97.5 (95.0, 99.9)	95.2 (92.4, 98.0)
12 months	97.5 (95.0, 99.9)	95.2 (92.4, 98.0)
18 months	NE (NE, NE)	95.2 (92.4, 98.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	2 (1.2)	10 (3.0)
Number of Subjects Censored, n (%)	164 (98.8)	322 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.686 (0.790)
95% CI		(0.359, 7.929)
Log-rank p-value		0.492

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (97.1, 100.0)	97.8 (96.2, 99.4)
6 months	98.8 (97.1, 100.0)	96.9 (94.6, 99.3)
9 months	98.8 (97.1, 100.0)	92.3 (85.5, 99.1)
12 months	98.8 (97.1, 100.0)	92.3 (85.5, 99.1)
18 months	NE (NE, NE)	92.3 (85.5, 99.1)
Median Follow-up Time (months)	2.81	3.96

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	0	9 (2.7)
Number of Subjects Censored, n (%)	166 (100.0)	323 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.048

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.0 (95.1, 98.9)
6 months	100.0 (100.0, 100.0)	97.0 (95.1, 98.9)
9 months	100.0 (100.0, 100.0)	97.0 (95.1, 98.9)
12 months	100.0 (100.0, 100.0)	97.0 (95.1, 98.9)
18 months	NE (NE, NE)	97.0 (95.1, 98.9)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	23 (13.9)	121 (36.4)
Number of Subjects Censored, n (%)	143 (86.1)	211 (63.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	1.48 (0.72, 1.84)
Median (95% CI)	NE (NE, NE)	13.14 (13.14, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.14, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.776 (0.231)
95% CI		(1.767, 4.364)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.2 (80.8, 91.6)	65.7 (60.4, 70.9)
6 months	83.0 (75.0, 91.0)	60.4 (54.3, 66.4)
9 months	83.0 (75.0, 91.0)	57.4 (50.4, 64.5)
12 months	83.0 (75.0, 91.0)	57.4 (50.4, 64.5)
18 months	NE (NE, NE)	28.7 (0.0, 68.7)
Median Follow-up Time (months)	2.60	2.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	6 (3.6)	69 (20.8)
Number of Subjects Censored, n (%)	160 (96.4)	263 (79.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.65, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.107 (0.433)
95% CI		(2.613, 14.271)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.2 (93.3, 99.2)	80.7 (76.4, 85.1)
6 months	96.2 (93.3, 99.2)	76.8 (71.6, 82.0)
9 months	96.2 (93.3, 99.2)	75.0 (68.9, 81.1)
12 months	96.2 (93.3, 99.2)	75.0 (68.9, 81.1)
18 months	NE (NE, NE)	75.0 (68.9, 81.1)
Median Follow-up Time (months)	2.79	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	8 (4.8)	14 (4.2)
Number of Subjects Censored, n (%)	158 (95.2)	318 (95.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.807 (0.445)
95% CI		(0.337, 1.930)
Log-rank p-value		0.640

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (91.7, 98.4)	95.5 (93.2, 97.8)
6 months	95.1 (91.7, 98.4)	95.5 (93.2, 97.8)
9 months	95.1 (91.7, 98.4)	95.5 (93.2, 97.8)
12 months	95.1 (91.7, 98.4)	95.5 (93.2, 97.8)
18 months	NE (NE, NE)	95.5 (93.2, 97.8)
Median Follow-up Time (months)	2.79	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	3 (1.8)	10 (3.0)
Number of Subjects Censored, n (%)	163 (98.2)	322 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.345 (0.665)
95% CI		(0.365, 4.954)
Log-rank p-value		0.666

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.8, 100.0)	97.1 (95.2, 99.0)
6 months	95.7 (89.6, 100.0)	96.6 (94.4, 98.7)
9 months	95.7 (89.6, 100.0)	96.6 (94.4, 98.7)
12 months	95.7 (89.6, 100.0)	96.6 (94.4, 98.7)
18 months	NE (NE, NE)	96.6 (94.4, 98.7)
Median Follow-up Time (months)	2.81	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	29 (17.5)	82 (24.7)
Number of Subjects Censored, n (%)	137 (82.5)	250 (75.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.50, NE)	4.86 (2.27, NE)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.199 (0.219)
95% CI		(0.781, 1.842)
Log-rank p-value		0.413

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.6 (74.1, 87.1)	78.0 (73.5, 82.6)
6 months	80.6 (74.1, 87.1)	72.4 (66.7, 78.2)
9 months	80.6 (74.1, 87.1)	70.3 (64.1, 76.6)
12 months	80.6 (74.1, 87.1)	64.5 (52.1, 76.9)
18 months	NE (NE, NE)	64.5 (52.1, 76.9)
Median Follow-up Time (months)	2.56	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	8 (4.8)	30 (9.0)
Number of Subjects Censored, n (%)	158 (95.2)	302 (91.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.1, 13.0*	0.0, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.638 (0.402)
95% CI		(0.745, 3.602)
Log-rank p-value		0.215

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.5 (90.7, 98.3)	92.1 (89.2, 95.0)
6 months	94.5 (90.7, 98.3)	91.4 (88.2, 94.6)
9 months	94.5 (90.7, 98.3)	89.4 (85.2, 93.6)
12 months	94.5 (90.7, 98.3)	89.4 (85.2, 93.6)
18 months	NE (NE, NE)	89.4 (85.2, 93.6)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	5 (3.0)	4 (1.2)
Number of Subjects Censored, n (%)	161 (97.0)	328 (98.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.364 (0.672)
95% CI		(0.098, 1.358)
Log-rank p-value		0.124

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (94.3, 99.6)	98.7 (97.5, 100.0)
6 months	96.9 (94.3, 99.6)	98.7 (97.5, 100.0)
9 months	96.9 (94.3, 99.6)	98.7 (97.5, 100.0)
12 months	96.9 (94.3, 99.6)	98.7 (97.5, 100.0)
18 months	NE (NE, NE)	98.7 (97.5, 100.0)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	3 (1.8)	8 (2.4)
Number of Subjects Censored, n (%)	163 (98.2)	324 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.231 (0.677)
95% CI		(0.326, 4.645)
Log-rank p-value		0.779

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (95.9, 100.0)	97.5 (95.9, 99.2)
6 months	98.0 (95.9, 100.0)	97.5 (95.9, 99.2)
9 months	98.0 (95.9, 100.0)	97.5 (95.9, 99.2)
12 months	98.0 (95.9, 100.0)	97.5 (95.9, 99.2)
18 months	NE (NE, NE)	97.5 (95.9, 99.2)
Median Follow-up Time (months)	2.79	3.96

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	24 (14.5)	88 (26.5)
Number of Subjects Censored, n (%)	142 (85.5)	244 (73.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	3.71 (2.73, 5.78)
Median (95% CI)	NE (NE, NE)	13.60 (11.96, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.480 (0.233)
95% CI		(0.937, 2.337)
Log-rank p-value		0.127

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.2 (78.1, 90.3)	77.7 (73.1, 82.4)
6 months	81.0 (72.4, 89.5)	68.9 (62.8, 75.0)
9 months	81.0 (72.4, 89.5)	66.7 (60.1, 73.3)
12 months	81.0 (72.4, 89.5)	57.2 (39.0, 75.4)
18 months	NE (NE, NE)	28.6 (0.0, 69.3)
Median Follow-up Time (months)	2.55	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	10 (6.0)	60 (18.1)
Number of Subjects Censored, n (%)	156 (94.0)	272 (81.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.60 (4.63, NE)
Median (95% CI)	NE (NE, NE)	13.60 (13.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.2*, 13.0*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.445 (0.345)
95% CI		(1.244, 4.805)
Log-rank p-value		0.009

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.4 (89.4, 97.4)	84.5 (80.4, 88.5)
6 months	93.4 (89.4, 97.4)	78.4 (73.1, 83.7)
9 months	93.4 (89.4, 97.4)	76.1 (69.3, 82.9)
12 months	93.4 (89.4, 97.4)	76.1 (69.3, 82.9)
18 months	NE (NE, NE)	38.1 (0.0, 90.9)
Median Follow-up Time (months)	2.74	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	3 (1.8)	6 (1.8)
Number of Subjects Censored, n (%)	163 (98.2)	326 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.851 (0.713)
95% CI		(0.210, 3.440)
Log-rank p-value		0.763

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (96.1, 100.0)	98.4 (97.1, 99.8)
6 months	98.1 (96.1, 100.0)	97.9 (96.1, 99.6)
9 months	98.1 (96.1, 100.0)	97.9 (96.1, 99.6)
12 months	98.1 (96.1, 100.0)	97.9 (96.1, 99.6)
18 months	NE (NE, NE)	97.9 (96.1, 99.6)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	23 (13.9)	70 (21.1)
Number of Subjects Censored, n (%)	143 (86.1)	262 (78.9)
Time to first TEAE (months)		
25% percentile (95% CI)	5.78 (4.34, NE)	5.91 (4.63, 7.69)
Median (95% CI)	NE (5.78, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.096 (0.250)
95% CI		(0.672, 1.788)
Log-rank p-value		0.715

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.6 (81.1, 92.1)	83.7 (79.5, 87.9)
6 months	69.6 (48.9, 90.3)	74.3 (68.1, 80.5)
9 months	69.6 (48.9, 90.3)	63.4 (54.0, 72.9)
12 months	69.6 (48.9, 90.3)	63.4 (54.0, 72.9)
18 months	NE (NE, NE)	63.4 (54.0, 72.9)
Median Follow-up Time (months)	2.78	3.20

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	5 (3.0)	12 (3.6)
Number of Subjects Censored, n (%)	161 (97.0)	320 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.786 (0.553)
95% CI		(0.266, 2.326)
Log-rank p-value		0.982

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (97.1, 100.0)	97.2 (95.4, 99.0)
6 months	88.4 (76.8, 100.0)	96.2 (93.6, 98.8)
9 months	88.4 (76.8, 100.0)	93.8 (89.5, 98.0)
12 months	88.4 (76.8, 100.0)	93.8 (89.5, 98.0)
18 months	NE (NE, NE)	93.8 (89.5, 98.0)
Median Follow-up Time (months)	2.81	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	5 (3.0)	7 (2.1)
Number of Subjects Censored, n (%)	161 (97.0)	325 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.345 (0.626)
95% CI		(0.101, 1.176)
Log-rank p-value		0.121

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (94.4, 99.9)	98.9 (97.8, 100.0)
6 months	92.9 (84.4, 100.0)	96.8 (94.1, 99.5)
9 months	92.9 (84.4, 100.0)	95.7 (92.2, 99.1)
12 months	92.9 (84.4, 100.0)	95.7 (92.2, 99.1)
18 months	NE (NE, NE)	95.7 (92.2, 99.1)
Median Follow-up Time (months)	2.79	3.96

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	1 (0.6)	11 (3.3)
Number of Subjects Censored, n (%)	165 (99.4)	321 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.617 (1.049)
95% CI		(0.591, 36.056)
Log-rank p-value		0.093

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	96.5 (94.4, 98.7)
6 months	99.4 (98.2, 100.0)	95.7 (93.0, 98.4)
9 months	99.4 (98.2, 100.0)	95.7 (93.0, 98.4)
12 months	99.4 (98.2, 100.0)	95.7 (93.0, 98.4)
18 months	NE (NE, NE)	95.7 (93.0, 98.4)
Median Follow-up Time (months)	2.83	3.96

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	29 (17.5)	50 (15.1)
Number of Subjects Censored, n (%)	137 (82.5)	282 (84.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.33, NE)	NE (6.77, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.681 (0.237)
95% CI		(0.428, 1.085)
Log-rank p-value		0.120

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.8 (73.1, 86.6)	86.6 (82.8, 90.4)
6 months	79.8 (73.1, 86.6)	82.2 (77.2, 87.3)
9 months	79.8 (73.1, 86.6)	79.9 (74.1, 85.7)
12 months	79.8 (73.1, 86.6)	79.9 (74.1, 85.7)
18 months	NE (NE, NE)	79.9 (74.1, 85.7)
Median Follow-up Time (months)	2.51	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	23 (13.9)	26 (7.8)
Number of Subjects Censored, n (%)	143 (86.1)	306 (92.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.400 (0.294)
95% CI		(0.225, 0.712)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.4 (77.0, 89.8)	93.7 (91.0, 96.5)
6 months	83.4 (77.0, 89.8)	89.2 (84.6, 93.7)
9 months	83.4 (77.0, 89.8)	88.1 (83.2, 93.0)
12 months	83.4 (77.0, 89.8)	88.1 (83.2, 93.0)
18 months	NE (NE, NE)	88.1 (83.2, 93.0)
Median Follow-up Time (months)	2.60	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	2 (1.2)	20 (6.0)
Number of Subjects Censored, n (%)	164 (98.8)	312 (94.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.729 (0.742)
95% CI		(1.104, 20.252)
Log-rank p-value		0.022

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.8, 100.0)	93.7 (91.1, 96.4)
6 months	98.7 (96.8, 100.0)	93.7 (91.1, 96.4)
9 months	98.7 (96.8, 100.0)	93.7 (91.1, 96.4)
12 months	98.7 (96.8, 100.0)	93.7 (91.1, 96.4)
18 months	NE (NE, NE)	93.7 (91.1, 96.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Endocrine disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	1 (0.6)	71 (21.4)
Number of Subjects Censored, n (%)	165 (99.4)	261 (78.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.59 (3.91, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		29.796 (1.008)
95% CI		(4.131, 214.912)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Endocrine disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	82.4 (78.1, 86.7)
6 months	99.4 (98.2, 100.0)	70.6 (63.7, 77.4)
9 months	99.4 (98.2, 100.0)	68.4 (61.1, 75.6)
12 months	99.4 (98.2, 100.0)	68.4 (61.1, 75.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	1 (0.6)	65 (19.6)
Number of Subjects Censored, n (%)	165 (99.4)	267 (80.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.78 (4.63, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		26.562 (1.009)
95% CI		(3.676, 191.949)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.2, 100.0)	84.3 (80.2, 88.4)
6 months	99.4 (98.2, 100.0)	73.3 (66.7, 80.0)
9 months	99.4 (98.2, 100.0)	69.4 (61.8, 77.1)
12 months	99.4 (98.2, 100.0)	69.4 (61.8, 77.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	11 (6.6)	41 (12.3)
Number of Subjects Censored, n (%)	155 (93.4)	291 (87.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.435 (0.344)
95% CI		(0.732, 2.815)
Log-rank p-value		0.287

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.7 (89.9, 97.5)	89.0 (85.4, 92.6)
6 months	91.5 (85.8, 97.1)	84.2 (79.3, 89.1)
9 months	91.5 (85.8, 97.1)	83.0 (77.7, 88.4)
12 months	91.5 (85.8, 97.1)	83.0 (77.7, 88.4)
18 months	NE (NE, NE)	83.0 (77.7, 88.4)
Median Follow-up Time (months)	2.79	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	7 (4.2)	21 (6.3)
Number of Subjects Censored, n (%)	159 (95.8)	311 (93.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.127 (0.442)
95% CI		(0.474, 2.681)
Log-rank p-value		0.737

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.6 (92.3, 98.8)	94.0 (91.2, 96.8)
6 months	95.6 (92.3, 98.8)	92.2 (88.8, 95.6)
9 months	95.6 (92.3, 98.8)	91.0 (86.9, 95.1)
12 months	95.6 (92.3, 98.8)	91.0 (86.9, 95.1)
18 months	NE (NE, NE)	91.0 (86.9, 95.1)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	2 (1.2)	6 (1.8)
Number of Subjects Censored, n (%)	164 (98.8)	326 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.252 (0.842)
95% CI		(0.241, 6.515)
Log-rank p-value		0.890

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	98.1 (96.5, 99.8)
6 months	97.0 (92.3, 100.0)	97.3 (95.1, 99.6)
9 months	97.0 (92.3, 100.0)	97.3 (95.1, 99.6)
12 months	97.0 (92.3, 100.0)	97.3 (95.1, 99.6)
18 months	NE (NE, NE)	97.3 (95.1, 99.6)
Median Follow-up Time (months)	2.81	3.96

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	1 (0.6)	4 (1.2)
Number of Subjects Censored, n (%)	165 (99.4)	328 (98.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.528 (1.128)
95% CI		(0.168, 13.939)
Log-rank p-value		0.745

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.1, 100.0)	99.0 (97.9, 100.0)
6 months	99.4 (98.1, 100.0)	98.2 (96.2, 100.0)
9 months	99.4 (98.1, 100.0)	98.2 (96.2, 100.0)
12 months	99.4 (98.1, 100.0)	98.2 (96.2, 100.0)
18 months	NE (NE, NE)	98.2 (96.2, 100.0)
Median Follow-up Time (months)	2.83	4.07

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	21 (12.7)	44 (13.3)
Number of Subjects Censored, n (%)	145 (87.3)	288 (86.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.846 (0.268)
95% CI		(0.500, 1.432)
Log-rank p-value		0.485

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.3 (82.0, 92.5)	87.5 (83.7, 91.2)
6 months	85.2 (78.7, 91.7)	83.3 (78.4, 88.2)
9 months	85.2 (78.7, 91.7)	83.3 (78.4, 88.2)
12 months	85.2 (78.7, 91.7)	83.3 (78.4, 88.2)
18 months	NE (NE, NE)	83.3 (78.4, 88.2)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	3 (1.8)	17 (5.1)
Number of Subjects Censored, n (%)	163 (98.2)	315 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.101 (0.631)
95% CI		(0.611, 7.231)
Log-rank p-value		0.241

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.9 (95.5, 100.0)	94.8 (92.2, 97.4)
6 months	97.9 (95.5, 100.0)	93.3 (90.1, 96.6)
9 months	97.9 (95.5, 100.0)	93.3 (90.1, 96.6)
12 months	97.9 (95.5, 100.0)	93.3 (90.1, 96.6)
18 months	NE (NE, NE)	93.3 (90.1, 96.6)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3K
Summary of Time to Onset of TEAE by SOC/PT by Number of Prior Chemotherapy Treatment Lines in Metastatic Disease
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
>3

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Number of Subjects with Events, n (%)	2 (1.2)	12 (3.6)
Number of Subjects Censored, n (%)	164 (98.8)	320 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.649 (0.770)
95% CI		(0.585, 11.990)
Log-rank p-value		0.234

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=166	Fruquintinib + BSC N=332
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (97.1, 100.0)	96.8 (94.9, 98.8)
6 months	98.8 (97.1, 100.0)	95.4 (92.6, 98.2)
9 months	98.8 (97.1, 100.0)	95.4 (92.6, 98.2)
12 months	98.8 (97.1, 100.0)	95.4 (92.6, 98.2)
18 months	NE (NE, NE)	95.4 (92.6, 98.2)
Median Follow-up Time (months)	2.83	3.94

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	124 (56.1)	304 (69.1)
Number of Subjects Censored, n (%)	97 (43.9)	136 (30.9)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.49, 0.69)	0.44 (0.30, 0.66)
Median (95% CI)	1.87 (1.35, 3.19)	1.18 (0.95, 1.61)
75% percentile (95% CI)	NE (NE, NE)	6.47 (4.60, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Min, Max	0.0, 13.0*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.254 (0.107)
95% CI		(1.016, 1.548)
Log-rank p-value		0.053

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	43.6 (36.8, 50.4)	37.3 (32.7, 41.9)
6 months	35.2 (25.0, 45.3)	25.6 (20.8, 30.5)
9 months	35.2 (25.0, 45.3)	21.3 (15.6, 27.0)
12 months	35.2 (25.0, 45.3)	21.3 (15.6, 27.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.61	1.12

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	51 (23.1)	151 (34.3)
Number of Subjects Censored, n (%)	170 (76.9)	289 (65.7)
Time to first TEAE (months)		
25% percentile (95% CI)	3.22 (1.28, NE)	1.35 (0.89, 1.74)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.431 (0.163)
95% CI		(1.040, 1.969)
Log-rank p-value		0.027

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.6 (70.7, 82.4)	67.4 (62.9, 71.9)
6 months	70.4 (59.9, 80.8)	63.3 (58.4, 68.3)
9 months	70.4 (59.9, 80.8)	60.4 (54.1, 66.8)
12 months	70.4 (59.9, 80.8)	60.4 (54.1, 66.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	34 (15.4)	88 (20.0)
Number of Subjects Censored, n (%)	187 (84.6)	352 (80.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.71, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.210 (0.203)
95% CI		(0.812, 1.802)
Log-rank p-value		0.377

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.5 (78.3, 88.6)	81.2 (77.5, 85.0)
6 months	83.5 (78.3, 88.6)	78.0 (73.8, 82.3)
9 months	83.5 (78.3, 88.6)	76.9 (72.1, 81.7)
12 months	83.5 (78.3, 88.6)	76.9 (72.1, 81.7)
18 months	NE (NE, NE)	76.9 (72.1, 81.7)
Median Follow-up Time (months)	2.60	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	23 (10.4)	43 (9.8)
Number of Subjects Censored, n (%)	198 (89.6)	397 (90.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.70, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.776 (0.264)
95% CI		(0.463, 1.302)
Log-rank p-value		0.303

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (84.5, 93.4)	91.8 (89.2, 94.4)
6 months	84.3 (74.4, 94.1)	89.4 (86.1, 92.7)
9 months	84.3 (74.4, 94.1)	87.9 (84.0, 91.7)
12 months	84.3 (74.4, 94.1)	82.7 (72.2, 93.2)
18 months	NE (NE, NE)	82.7 (72.2, 93.2)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	6 (2.7)	57 (13.0)
Number of Subjects Censored, n (%)	215 (97.3)	383 (87.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
Median (95% CI)	NE (NE, NE)	NE (13.24, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.24, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.548 (0.431)
95% CI		(1.955, 10.582)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (94.8, 99.4)	88.2 (85.1, 91.2)
6 months	97.1 (94.8, 99.4)	86.9 (83.5, 90.2)
9 months	97.1 (94.8, 99.4)	84.6 (80.1, 89.1)
12 months	97.1 (94.8, 99.4)	84.6 (80.1, 89.1)
18 months	NE (NE, NE)	56.4 (11.2, 100.0)
Median Follow-up Time (months)	2.83	3.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	27 (12.2)	27 (6.1)
Number of Subjects Censored, n (%)	194 (87.8)	413 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.356 (0.280)
95% CI		(0.206, 0.616)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.2 (82.4, 91.9)	95.9 (94.0, 97.8)
6 months	83.5 (76.8, 90.3)	91.7 (88.4, 95.0)
9 months	83.5 (76.8, 90.3)	91.7 (88.4, 95.0)
12 months	83.5 (76.8, 90.3)	91.7 (88.4, 95.0)
18 months	NE (NE, NE)	84.7 (71.0, 98.3)
Median Follow-up Time (months)	2.83	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	17 (7.7)	22 (5.0)
Number of Subjects Censored, n (%)	204 (92.3)	418 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.560 (0.329)
95% CI		(0.294, 1.067)
Log-rank p-value		0.069

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.8 (88.1, 95.6)	95.2 (93.2, 97.3)
6 months	91.8 (88.1, 95.6)	95.2 (93.2, 97.3)
9 months	91.8 (88.1, 95.6)	93.0 (88.3, 97.8)
12 months	91.8 (88.1, 95.6)	89.8 (82.1, 97.5)
18 months	NE (NE, NE)	89.8 (82.1, 97.5)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	5 (2.3)	15 (3.4)
Number of Subjects Censored, n (%)	216 (97.7)	425 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.82, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.918 (0.542)
95% CI		(0.317, 2.658)
Log-rank p-value		0.798

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (95.4, 99.7)	98.1 (96.8, 99.4)
6 months	97.6 (95.4, 99.7)	96.7 (94.6, 98.8)
9 months	97.6 (95.4, 99.7)	95.3 (92.0, 98.7)
12 months	97.6 (95.4, 99.7)	87.2 (77.8, 96.6)
18 months	NE (NE, NE)	87.2 (77.8, 96.6)
Median Follow-up Time (months)	2.83	3.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	4 (1.8)	11 (2.5)
Number of Subjects Censored, n (%)	217 (98.2)	429 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.966 (0.597)
95% CI		(0.299, 3.115)
Log-rank p-value		0.894

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (95.4, 100.0)	98.0 (96.6, 99.4)
6 months	97.7 (95.4, 100.0)	97.0 (95.1, 98.9)
9 months	97.7 (95.4, 100.0)	95.6 (92.3, 98.9)
12 months	97.7 (95.4, 100.0)	95.6 (92.3, 98.9)
18 months	NE (NE, NE)	95.6 (92.3, 98.9)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	2 (0.9)	11 (2.5)
Number of Subjects Censored, n (%)	219 (99.1)	429 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.173 (0.782)
95% CI		(0.469, 10.071)
Log-rank p-value		0.289

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.8, 100.0)	98.2 (96.9, 99.4)
6 months	99.1 (97.8, 100.0)	97.0 (94.9, 99.1)
9 months	99.1 (97.8, 100.0)	95.0 (90.5, 99.4)
12 months	99.1 (97.8, 100.0)	95.0 (90.5, 99.4)
18 months	NE (NE, NE)	95.0 (90.5, 99.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	127 (57.5)	295 (67.0)
Number of Subjects Censored, n (%)	94 (42.5)	145 (33.0)
Time to first TEAE (months)		
25% percentile (95% CI)	0.56 (0.39, 0.69)	0.51 (0.46, 0.69)
Median (95% CI)	1.61 (1.31, 2.27)	1.45 (1.02, 1.87)
75% percentile (95% CI)	5.59 (4.34, NE)	6.70 (4.90, 10.12)
Min, Max	0.0, 6.4*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.044 (0.108)
95% CI		(0.845, 1.290)
Log-rank p-value		0.636

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	40.6 (33.4, 47.9)	39.2 (34.5, 43.9)
6 months	19.7 (4.3, 35.0)	26.2 (20.9, 31.5)
9 months	NE (NE, NE)	19.8 (13.7, 25.9)
12 months	NE (NE, NE)	17.0 (9.7, 24.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.38	1.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	22 (10.0)	105 (23.9)
Number of Subjects Censored, n (%)	199 (90.0)	335 (76.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.55 (2.89, 7.33)
Median (95% CI)	NE (NE, NE)	NE (10.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.154 (0.237)
95% CI		(1.354, 3.425)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.7 (85.6, 93.8)	79.1 (75.2, 83.0)
6 months	89.7 (85.6, 93.8)	73.1 (68.0, 78.2)
9 months	89.7 (85.6, 93.8)	69.2 (63.1, 75.3)
12 months	89.7 (85.6, 93.8)	63.4 (51.2, 75.6)
18 months	NE (NE, NE)	63.4 (51.2, 75.6)
Median Follow-up Time (months)	2.76	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	41 (18.6)	75 (17.0)
Number of Subjects Censored, n (%)	180 (81.4)	365 (83.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.79, NE)	9.00 (5.68, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.699 (0.199)
95% CI		(0.473, 1.033)
Log-rank p-value		0.072

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.0 (75.6, 86.4)	84.8 (81.3, 88.4)
6 months	77.5 (69.0, 86.0)	79.9 (75.3, 84.6)
9 months	77.5 (69.0, 86.0)	76.9 (71.2, 82.5)
12 months	77.5 (69.0, 86.0)	74.7 (67.8, 81.6)
18 months	NE (NE, NE)	74.7 (67.8, 81.6)
Median Follow-up Time (months)	2.69	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	36 (16.3)	80 (18.2)
Number of Subjects Censored, n (%)	185 (83.7)	360 (81.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.57, NE)	7.98 (5.52, NE)
Median (95% CI)	NE (NE, NE)	NE (12.25, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.854 (0.205)
95% CI		(0.572, 1.277)
Log-rank p-value		0.500

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.0 (76.3, 87.7)	84.6 (81.0, 88.1)
6 months	78.7 (70.4, 87.1)	79.8 (75.4, 84.3)
9 months	78.7 (70.4, 87.1)	74.7 (68.6, 80.9)
12 months	78.7 (70.4, 87.1)	71.5 (62.9, 80.0)
18 months	NE (NE, NE)	62.5 (44.5, 80.6)
Median Follow-up Time (months)	2.79	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	22 (10.0)	77 (17.5)
Number of Subjects Censored, n (%)	199 (90.0)	363 (82.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	9.33 (5.82, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.384 (0.245)
95% CI		(0.856, 2.239)
Log-rank p-value		0.198

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (84.0, 93.8)	85.0 (81.5, 88.5)
6 months	87.3 (81.5, 93.0)	79.2 (74.6, 83.9)
9 months	87.3 (81.5, 93.0)	76.0 (70.2, 81.7)
12 months	87.3 (81.5, 93.0)	73.6 (66.4, 80.8)
18 months	NE (NE, NE)	73.6 (66.4, 80.8)
Median Follow-up Time (months)	2.79	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	26 (11.8)	63 (14.3)
Number of Subjects Censored, n (%)	195 (88.2)	377 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.36, NE)	18.04 (7.39, NE)
Median (95% CI)	NE (NE, NE)	NE (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.913 (0.239)
95% CI		(0.571, 1.459)
Log-rank p-value		0.707

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.3 (83.8, 92.7)	88.7 (85.7, 91.8)
6 months	81.4 (70.7, 92.1)	83.7 (79.4, 87.9)
9 months	81.4 (70.7, 92.1)	79.8 (74.2, 85.3)
12 months	81.4 (70.7, 92.1)	76.8 (69.0, 84.6)
18 months	NE (NE, NE)	76.8 (69.0, 84.6)
Median Follow-up Time (months)	2.83	3.56

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	8 (3.6)	63 (14.3)
Number of Subjects Censored, n (%)	213 (96.4)	377 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.821 (0.377)
95% CI		(1.826, 7.994)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.0 (93.3, 98.7)	86.8 (83.6, 90.0)
6 months	96.0 (93.3, 98.7)	84.9 (81.3, 88.6)
9 months	96.0 (93.3, 98.7)	82.6 (77.8, 87.4)
12 months	96.0 (93.3, 98.7)	82.6 (77.8, 87.4)
18 months	NE (NE, NE)	82.6 (77.8, 87.4)
Median Follow-up Time (months)	2.83	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	8 (3.6)	32 (7.3)
Number of Subjects Censored, n (%)	213 (96.4)	408 (92.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.624 (0.401)
95% CI		(0.741, 3.562)
Log-rank p-value		0.238

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.7 (94.2, 99.1)	93.8 (91.5, 96.1)
6 months	90.6 (78.9, 100.0)	91.6 (88.6, 94.6)
9 months	NE (NE, NE)	90.2 (86.1, 94.2)
12 months	NE (NE, NE)	90.2 (86.1, 94.2)
18 months	NE (NE, NE)	90.2 (86.1, 94.2)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	4 (1.8)	16 (3.6)
Number of Subjects Censored, n (%)	217 (98.2)	424 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.642 (0.568)
95% CI		(0.539, 5.001)
Log-rank p-value		0.365

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (96.2, 99.9)	97.0 (95.4, 98.6)
6 months	98.1 (96.2, 99.9)	95.8 (93.6, 98.1)
9 months	98.1 (96.2, 99.9)	94.5 (91.0, 97.9)
12 months	98.1 (96.2, 99.9)	94.5 (91.0, 97.9)
18 months	NE (NE, NE)	94.5 (91.0, 97.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	4 (1.8)	11 (2.5)
Number of Subjects Censored, n (%)	217 (98.2)	429 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.257 (0.586)
95% CI		(0.399, 3.963)
Log-rank p-value		0.679

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.9 (95.9, 100.0)	97.3 (95.8, 98.9)
6 months	97.9 (95.9, 100.0)	97.3 (95.8, 98.9)
9 months	97.9 (95.9, 100.0)	97.3 (95.8, 98.9)
12 months	97.9 (95.9, 100.0)	97.3 (95.8, 98.9)
18 months	NE (NE, NE)	97.3 (95.8, 98.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	10 (4.5)	3 (0.7)
Number of Subjects Censored, n (%)	211 (95.5)	437 (99.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.116 (0.683)
95% CI		(0.030, 0.441)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (92.0, 98.1)	99.5 (98.8, 100.0)
6 months	95.1 (92.0, 98.1)	98.8 (97.2, 100.0)
9 months	95.1 (92.0, 98.1)	98.8 (97.2, 100.0)
12 months	95.1 (92.0, 98.1)	98.8 (97.2, 100.0)
18 months	NE (NE, NE)	98.8 (97.2, 100.0)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	0	11 (2.5)
Number of Subjects Censored, n (%)	221 (100.0)	429 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.028

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.5 (96.0, 99.1)
6 months	100.0 (100.0, 100.0)	97.5 (96.0, 99.1)
9 months	100.0 (100.0, 100.0)	96.0 (92.8, 99.3)
12 months	100.0 (100.0, 100.0)	96.0 (92.8, 99.3)
18 months	NE (NE, NE)	96.0 (92.8, 99.3)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	59 (26.7)	190 (43.2)
Number of Subjects Censored, n (%)	162 (73.3)	250 (56.8)
Time to first TEAE (months)		
25% percentile (95% CI)	1.91 (0.95, NE)	1.35 (0.95, 1.64)
Median (95% CI)	10.18 (NE, NE)	6.44 (4.73, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.0, 10.2	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.455 (0.150)
95% CI		(1.084, 1.954)
Log-rank p-value		0.014

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.3 (67.3, 79.4)	59.6 (54.9, 64.4)
6 months	68.2 (59.0, 77.4)	53.3 (47.9, 58.6)
9 months	68.2 (59.0, 77.4)	48.3 (42.0, 54.6)
12 months	0.0 (NE, NE)	45.4 (37.4, 53.5)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.46	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	39 (17.6)	120 (27.3)
Number of Subjects Censored, n (%)	182 (82.4)	320 (72.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.27, NE)	2.89 (1.91, 5.36)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.402 (0.186)
95% CI		(0.974, 2.019)
Log-rank p-value		0.079

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.8 (76.5, 87.1)	73.7 (69.4, 78.0)
6 months	78.6 (70.7, 86.5)	70.1 (65.3, 74.9)
9 months	78.6 (70.7, 86.5)	68.6 (63.5, 73.7)
12 months	78.6 (70.7, 86.5)	66.1 (59.3, 73.0)
18 months	NE (NE, NE)	66.1 (59.3, 73.0)
Median Follow-up Time (months)	2.76	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	4 (1.8)	28 (6.4)
Number of Subjects Censored, n (%)	217 (98.2)	412 (93.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.908 (0.537)
95% CI		(1.014, 8.337)
Log-rank p-value		0.037

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (96.4, 99.9)	93.7 (91.3, 96.1)
6 months	98.2 (96.4, 99.9)	92.9 (90.2, 95.5)
9 months	98.2 (96.4, 99.9)	91.5 (87.8, 95.2)
12 months	98.2 (96.4, 99.9)	91.5 (87.8, 95.2)
18 months	NE (NE, NE)	91.5 (87.8, 95.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	5 (2.3)	20 (4.5)
Number of Subjects Censored, n (%)	216 (97.7)	420 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.450 (0.510)
95% CI		(0.533, 3.941)
Log-rank p-value		0.419

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (96.3, 99.9)	96.4 (94.5, 98.2)
6 months	96.4 (92.5, 100.0)	94.2 (91.4, 97.0)
9 months	96.4 (92.5, 100.0)	93.0 (89.4, 96.6)
12 months	96.4 (92.5, 100.0)	93.0 (89.4, 96.6)
18 months	NE (NE, NE)	93.0 (89.4, 96.6)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	4 (1.8)	13 (3.0)
Number of Subjects Censored, n (%)	217 (98.2)	427 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.321 (0.579)
95% CI		(0.424, 4.113)
Log-rank p-value		0.604

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (96.0, 100.0)	97.3 (95.7, 98.9)
6 months	98.0 (96.0, 100.0)	96.9 (95.1, 98.7)
9 months	98.0 (96.0, 100.0)	94.9 (90.7, 99.1)
12 months	98.0 (96.0, 100.0)	94.9 (90.7, 99.1)
18 months	NE (NE, NE)	94.9 (90.7, 99.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	3 (1.4)	15 (3.4)
Number of Subjects Censored, n (%)	218 (98.6)	425 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.087 (0.638)
95% CI		(0.597, 7.292)
Log-rank p-value		0.235

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (97.1, 100.0)	96.8 (95.1, 98.5)
6 months	98.6 (97.1, 100.0)	96.2 (94.1, 98.3)
9 months	98.6 (97.1, 100.0)	94.9 (91.7, 98.1)
12 months	98.6 (97.1, 100.0)	94.9 (91.7, 98.1)
18 months	NE (NE, NE)	94.9 (91.7, 98.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	0	16 (3.6)
Number of Subjects Censored, n (%)	221 (100.0)	424 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.009

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.7 (94.9, 98.4)
6 months	100.0 (100.0, 100.0)	96.1 (94.2, 98.1)
9 months	100.0 (100.0, 100.0)	95.0 (92.0, 98.0)
12 months	100.0 (100.0, 100.0)	95.0 (92.0, 98.0)
18 months	NE (NE, NE)	95.0 (92.0, 98.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	2 (0.9)	13 (3.0)
Number of Subjects Censored, n (%)	219 (99.1)	427 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.600 (0.764)
95% CI		(0.582, 11.621)
Log-rank p-value		0.195

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.8, 100.0)	97.1 (95.4, 98.7)
6 months	98.7 (96.8, 100.0)	97.1 (95.4, 98.7)
9 months	98.7 (96.8, 100.0)	96.3 (94.0, 98.5)
12 months	98.7 (96.8, 100.0)	96.3 (94.0, 98.5)
18 months	NE (NE, NE)	96.3 (94.0, 98.5)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	2 (0.9)	13 (3.0)
Number of Subjects Censored, n (%)	219 (99.1)	427 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.393 (0.772)
95% CI		(0.527, 10.858)
Log-rank p-value		0.221

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.8, 100.0)	97.8 (96.4, 99.2)
6 months	99.1 (97.8, 100.0)	96.8 (94.7, 98.8)
9 months	99.1 (97.8, 100.0)	94.1 (89.6, 98.6)
12 months	99.1 (97.8, 100.0)	94.1 (89.6, 98.6)
18 months	NE (NE, NE)	94.1 (89.6, 98.6)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	2 (0.9)	11 (2.5)
Number of Subjects Censored, n (%)	219 (99.1)	429 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Median (95% CI)	10.18 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 10.2	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.210 (0.777)
95% CI		(0.482, 10.132)
Log-rank p-value		0.308

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.6, 100.0)	97.4 (95.8, 98.9)
6 months	99.5 (98.6, 100.0)	97.4 (95.8, 98.9)
9 months	99.5 (98.6, 100.0)	97.4 (95.8, 98.9)
12 months	0.0 (NE, NE)	97.4 (95.8, 98.9)
18 months	0.0 (NE, NE)	97.4 (95.8, 98.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	1 (0.5)	11 (2.5)
Number of Subjects Censored, n (%)	220 (99.5)	429 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.084 (1.057)
95% CI		(0.389, 24.469)
Log-rank p-value		0.268

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.5, 100.0)	98.7 (97.5, 99.9)
6 months	99.5 (98.5, 100.0)	95.4 (92.6, 98.3)
9 months	99.5 (98.5, 100.0)	95.4 (92.6, 98.3)
12 months	99.5 (98.5, 100.0)	95.4 (92.6, 98.3)
18 months	NE (NE, NE)	95.4 (92.6, 98.3)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	60 (27.1)	181 (41.1)
Number of Subjects Censored, n (%)	161 (72.9)	259 (58.9)
Time to first TEAE (months)		
25% percentile (95% CI)	1.94 (1.18, 5.59)	1.58 (0.95, 1.64)
Median (95% CI)	NE (5.59, NE)	7.16 (5.78, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (16.79, NE)
Min, Max	0.0, 6.8*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.327 (0.151)
95% CI		(0.987, 1.784)
Log-rank p-value		0.067

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.9 (66.8, 79.1)	62.6 (57.9, 67.3)
6 months	54.3 (34.7, 73.9)	55.5 (50.0, 61.0)
9 months	NE (NE, NE)	47.9 (41.1, 54.7)
12 months	NE (NE, NE)	47.9 (41.1, 54.7)
18 months	NE (NE, NE)	35.9 (15.0, 56.9)
Median Follow-up Time (months)	2.63	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	21 (9.5)	56 (12.7)
Number of Subjects Censored, n (%)	200 (90.5)	384 (87.3)
Time to first TEAE (months)		
25% percentile (95% CI)	5.82 (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.82, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.066 (0.261)
95% CI		(0.639, 1.778)
Log-rank p-value		0.834

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.4 (84.8, 94.0)	88.9 (85.8, 91.9)
6 months	73.4 (51.7, 95.0)	85.1 (81.0, 89.1)
9 months	NE (NE, NE)	82.0 (76.7, 87.3)
12 months	NE (NE, NE)	82.0 (76.7, 87.3)
18 months	NE (NE, NE)	82.0 (76.7, 87.3)
Median Follow-up Time (months)	2.79	3.63

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	11 (5.0)	47 (10.7)
Number of Subjects Censored, n (%)	210 (95.0)	393 (89.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.680 (0.340)
95% CI		(0.862, 3.274)
Log-rank p-value		0.135

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.3 (92.5, 98.2)	90.7 (87.8, 93.6)
6 months	89.4 (77.7, 100.0)	87.6 (83.9, 91.3)
9 months	NE (NE, NE)	84.8 (79.9, 89.6)
12 months	NE (NE, NE)	84.8 (79.9, 89.6)
18 months	NE (NE, NE)	84.8 (79.9, 89.6)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	9 (4.1)	46 (10.5)
Number of Subjects Censored, n (%)	212 (95.9)	394 (89.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.987 (0.370)
95% CI		(0.962, 4.104)
Log-rank p-value		0.059

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.3 (93.8, 98.8)	91.3 (88.5, 94.0)
6 months	90.3 (78.6, 100.0)	88.4 (84.9, 91.9)
9 months	NE (NE, NE)	84.7 (79.7, 89.7)
12 months	NE (NE, NE)	84.7 (79.7, 89.7)
18 months	NE (NE, NE)	84.7 (79.7, 89.7)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	11 (5.0)	36 (8.2)
Number of Subjects Censored, n (%)	210 (95.0)	404 (91.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.247 (0.350)
95% CI		(0.628, 2.476)
Log-rank p-value		0.612

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (92.0, 97.8)	93.5 (91.1, 95.9)
6 months	94.9 (92.0, 97.8)	90.3 (87.0, 93.6)
9 months	94.9 (92.0, 97.8)	88.2 (83.9, 92.5)
12 months	94.9 (92.0, 97.8)	88.2 (83.9, 92.5)
18 months	NE (NE, NE)	88.2 (83.9, 92.5)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	3 (1.4)	30 (6.8)
Number of Subjects Censored, n (%)	218 (98.6)	410 (93.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.157 (0.609)
95% CI		(1.259, 13.721)
Log-rank p-value		0.013

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (97.4, 100.0)	93.6 (91.3, 96.0)
6 months	96.5 (91.7, 100.0)	92.3 (89.3, 95.3)
9 months	96.5 (91.7, 100.0)	89.7 (84.8, 94.6)
12 months	96.5 (91.7, 100.0)	89.7 (84.8, 94.6)
18 months	NE (NE, NE)	89.7 (84.8, 94.6)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	9 (4.1)	24 (5.5)
Number of Subjects Censored, n (%)	212 (95.9)	416 (94.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.061 (0.398)
95% CI		(0.486, 2.315)
Log-rank p-value		0.922

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (92.5, 98.4)	95.2 (93.1, 97.3)
6 months	95.4 (92.5, 98.4)	93.4 (90.6, 96.3)
9 months	95.4 (92.5, 98.4)	92.6 (89.4, 95.9)
12 months	95.4 (92.5, 98.4)	92.6 (89.4, 95.9)
18 months	NE (NE, NE)	92.6 (89.4, 95.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	2 (0.9)	27 (6.1)
Number of Subjects Censored, n (%)	219 (99.1)	413 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	7.43 (7.43, NE)	NE (NE, NE)
Median (95% CI)	7.43 (7.43, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (7.43, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.521 (0.736)
95% CI		(1.305, 23.352)
Log-rank p-value		0.009

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.7, 100.0)	94.2 (91.9, 96.5)
6 months	99.5 (98.7, 100.0)	92.7 (89.9, 95.5)
9 months	NE (NE, NE)	92.7 (89.9, 95.5)
12 months	NE (NE, NE)	92.7 (89.9, 95.5)
18 months	NE (NE, NE)	92.7 (89.9, 95.5)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	5 (2.3)	19 (4.3)
Number of Subjects Censored, n (%)	216 (97.7)	421 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.484 (0.509)
95% CI		(0.547, 4.021)
Log-rank p-value		0.452

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.7, 100.0)	96.0 (94.1, 97.9)
6 months	95.6 (90.7, 100.0)	94.9 (92.5, 97.4)
9 months	95.6 (90.7, 100.0)	94.2 (91.4, 97.0)
12 months	95.6 (90.7, 100.0)	94.2 (91.4, 97.0)
18 months	NE (NE, NE)	94.2 (91.4, 97.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	1 (0.5)	13 (3.0)
Number of Subjects Censored, n (%)	220 (99.5)	427 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.100 (1.044)
95% CI		(0.660, 39.442)
Log-rank p-value		0.086

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.6, 100.0)	97.2 (95.5, 98.8)
6 months	99.5 (98.6, 100.0)	96.7 (94.7, 98.6)
9 months	99.5 (98.6, 100.0)	95.6 (92.7, 98.4)
12 months	99.5 (98.6, 100.0)	95.6 (92.7, 98.4)
18 months	NE (NE, NE)	95.6 (92.7, 98.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	2 (0.9)	11 (2.5)
Number of Subjects Censored, n (%)	219 (99.1)	429 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.379 (0.775)
95% CI		(0.521, 10.862)
Log-rank p-value		0.253

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.8, 100.0)	97.5 (96.0, 99.0)
6 months	99.1 (97.8, 100.0)	97.5 (96.0, 99.0)
9 months	99.1 (97.8, 100.0)	96.4 (93.8, 99.0)
12 months	99.1 (97.8, 100.0)	96.4 (93.8, 99.0)
18 months	NE (NE, NE)	96.4 (93.8, 99.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	56 (25.3)	170 (38.6)
Number of Subjects Censored, n (%)	165 (74.7)	270 (61.4)
Time to first TEAE (months)		
25% percentile (95% CI)	2.40 (1.25, NE)	0.72 (0.69, 1.45)
Median (95% CI)	NE (NE, NE)	11.53 (9.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.498 (0.156)
95% CI		(1.104, 2.033)
Log-rank p-value		0.010

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.9 (66.7, 79.1)	64.6 (60.1, 69.1)
6 months	72.9 (66.7, 79.1)	59.5 (54.4, 64.6)
9 months	72.9 (66.7, 79.1)	57.3 (51.8, 62.8)
12 months	72.9 (66.7, 79.1)	48.4 (37.5, 59.4)
18 months	NE (NE, NE)	48.4 (37.5, 59.4)
Median Follow-up Time (months)	2.40	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	12 (5.4)	73 (16.6)
Number of Subjects Censored, n (%)	209 (94.6)	367 (83.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.283 (0.313)
95% CI		(1.778, 6.061)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.1 (90.9, 97.4)	83.4 (79.9, 86.9)
6 months	94.1 (90.9, 97.4)	83.0 (79.4, 86.6)
9 months	94.1 (90.9, 97.4)	83.0 (79.4, 86.6)
12 months	94.1 (90.9, 97.4)	83.0 (79.4, 86.6)
18 months	NE (NE, NE)	83.0 (79.4, 86.6)
Median Follow-up Time (months)	2.83	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	21 (9.5)	41 (9.3)
Number of Subjects Censored, n (%)	200 (90.5)	399 (90.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	14.32 (14.32, NE)
Median (95% CI)	NE (NE, NE)	NE (14.32, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.790 (0.274)
95% CI		(0.462, 1.350)
Log-rank p-value		0.405

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.0 (86.0, 94.1)	92.1 (89.5, 94.7)
6 months	90.0 (86.0, 94.1)	89.9 (86.7, 93.1)
9 months	90.0 (86.0, 94.1)	88.4 (84.7, 92.2)
12 months	90.0 (86.0, 94.1)	88.4 (84.7, 92.2)
18 months	NE (NE, NE)	73.7 (47.1, 100.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	21 (9.5)	37 (8.4)
Number of Subjects Censored, n (%)	200 (90.5)	403 (91.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.757 (0.278)
95% CI		(0.440, 1.305)
Log-rank p-value		0.315

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.8 (85.7, 94.0)	92.2 (89.6, 94.8)
6 months	89.8 (85.7, 94.0)	91.3 (88.4, 94.1)
9 months	89.8 (85.7, 94.0)	90.5 (87.3, 93.7)
12 months	89.8 (85.7, 94.0)	85.2 (74.6, 95.7)
18 months	NE (NE, NE)	85.2 (74.6, 95.7)
Median Follow-up Time (months)	2.76	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	3 (1.4)	17 (3.9)
Number of Subjects Censored, n (%)	218 (98.6)	423 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.642 (0.628)
95% CI		(0.772, 9.038)
Log-rank p-value		0.119

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (97.1, 100.0)	96.0 (94.1, 97.9)
6 months	98.6 (97.1, 100.0)	96.0 (94.1, 97.9)
9 months	98.6 (97.1, 100.0)	96.0 (94.1, 97.9)
12 months	98.6 (97.1, 100.0)	96.0 (94.1, 97.9)
18 months	NE (NE, NE)	96.0 (94.1, 97.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	2 (0.9)	10 (2.3)
Number of Subjects Censored, n (%)	219 (99.1)	430 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.845 (0.792)
95% CI		(0.391, 8.709)
Log-rank p-value		0.454

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.6, 100.0)	98.4 (97.2, 99.6)
6 months	99.0 (97.6, 100.0)	97.8 (96.1, 99.4)
9 months	99.0 (97.6, 100.0)	95.9 (92.8, 99.0)
12 months	99.0 (97.6, 100.0)	95.9 (92.8, 99.0)
18 months	NE (NE, NE)	95.9 (92.8, 99.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Vascular disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	32 (14.5)	171 (38.9)
Number of Subjects Censored, n (%)	189 (85.5)	269 (61.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.61, NE)	0.95 (0.69, 1.58)
Median (95% CI)	NE (NE, NE)	NE (7.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.816 (0.193)
95% CI		(1.928, 4.114)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Vascular disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.8 (79.9, 89.8)	62.3 (57.6, 66.9)
6 months	82.3 (75.3, 89.2)	58.5 (53.4, 63.7)
9 months	NE (NE, NE)	53.9 (47.4, 60.4)
12 months	NE (NE, NE)	53.9 (47.4, 60.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.63	2.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	19 (8.6)	160 (36.4)
Number of Subjects Censored, n (%)	202 (91.4)	280 (63.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.05 (0.72, 1.61)
Median (95% CI)	NE (NE, NE)	NE (7.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.516 (0.243)
95% CI		(2.803, 7.275)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.6 (86.5, 94.7)	64.6 (60.0, 69.2)
6 months	90.6 (86.5, 94.7)	62.2 (57.2, 67.1)
9 months	NE (NE, NE)	56.3 (49.6, 62.9)
12 months	NE (NE, NE)	56.3 (49.6, 62.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	47 (21.3)	146 (33.2)
Number of Subjects Censored, n (%)	174 (78.7)	294 (66.8)
Time to first TEAE (months)		
25% percentile (95% CI)	3.71 (1.87, NE)	1.68 (1.05, 2.46)
Median (95% CI)	NE (5.59, NE)	NE (9.76, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.440 (0.169)
95% CI		(1.034, 2.006)
Log-rank p-value		0.029

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.4 (72.6, 84.2)	68.3 (63.8, 72.7)
6 months	66.3 (50.6, 81.9)	63.6 (58.4, 68.9)
9 months	NE (NE, NE)	59.4 (52.4, 66.3)
12 months	NE (NE, NE)	56.5 (48.0, 65.1)
18 months	NE (NE, NE)	56.5 (48.0, 65.1)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	17 (7.7)	45 (10.2)
Number of Subjects Censored, n (%)	204 (92.3)	395 (89.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.093 (0.288)
95% CI		(0.622, 1.923)
Log-rank p-value		0.652

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.0 (88.3, 95.6)	90.5 (87.6, 93.3)
6 months	92.0 (88.3, 95.6)	88.0 (84.5, 91.5)
9 months	92.0 (88.3, 95.6)	87.2 (83.4, 91.0)
12 months	92.0 (88.3, 95.6)	87.2 (83.4, 91.0)
18 months	NE (NE, NE)	87.2 (83.4, 91.0)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	10 (4.5)	48 (10.9)
Number of Subjects Censored, n (%)	211 (95.5)	392 (89.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.002 (0.352)
95% CI		(1.004, 3.989)
Log-rank p-value		0.047

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (93.0, 98.5)	90.5 (87.7, 93.3)
6 months	89.7 (78.1, 100.0)	87.8 (84.1, 91.4)
9 months	NE (NE, NE)	84.0 (78.5, 89.5)
12 months	NE (NE, NE)	84.0 (78.5, 89.5)
18 months	NE (NE, NE)	84.0 (78.5, 89.5)
Median Follow-up Time (months)	2.83	3.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	5 (2.3)	26 (5.9)
Number of Subjects Censored, n (%)	216 (97.7)	414 (94.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.261 (0.491)
95% CI		(0.863, 5.921)
Log-rank p-value		0.082

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.8, 100.0)	94.3 (92.1, 96.5)
6 months	93.8 (87.3, 100.0)	93.0 (90.2, 95.9)
9 months	93.8 (87.3, 100.0)	93.0 (90.2, 95.9)
12 months	93.8 (87.3, 100.0)	93.0 (90.2, 95.9)
18 months	NE (NE, NE)	93.0 (90.2, 95.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	5 (2.3)	14 (3.2)
Number of Subjects Censored, n (%)	216 (97.7)	426 (96.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.224 (0.526)
95% CI		(0.436, 3.432)
Log-rank p-value		0.732

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (95.6, 99.7)	96.9 (95.2, 98.6)
6 months	97.6 (95.6, 99.7)	96.1 (93.9, 98.3)
9 months	97.6 (95.6, 99.7)	96.1 (93.9, 98.3)
12 months	97.6 (95.6, 99.7)	96.1 (93.9, 98.3)
18 months	NE (NE, NE)	96.1 (93.9, 98.3)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	2 (0.9)	11 (2.5)
Number of Subjects Censored, n (%)	219 (99.1)	429 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.022 (0.786)
95% CI		(0.433, 9.436)
Log-rank p-value		0.334

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.8, 100.0)	98.1 (96.8, 99.4)
6 months	99.1 (97.8, 100.0)	98.1 (96.8, 99.4)
9 months	99.1 (97.8, 100.0)	93.7 (88.5, 99.0)
12 months	99.1 (97.8, 100.0)	93.7 (88.5, 99.0)
18 months	NE (NE, NE)	93.7 (88.5, 99.0)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	0	11 (2.5)
Number of Subjects Censored, n (%)	221 (100.0)	429 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.029

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.3 (95.7, 98.9)
6 months	100.0 (100.0, 100.0)	97.3 (95.7, 98.9)
9 months	100.0 (100.0, 100.0)	97.3 (95.7, 98.9)
12 months	100.0 (100.0, 100.0)	97.3 (95.7, 98.9)
18 months	NE (NE, NE)	97.3 (95.7, 98.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	26 (11.8)	153 (34.8)
Number of Subjects Censored, n (%)	195 (88.2)	287 (65.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.51 (0.95, 1.84)
Median (95% CI)	NE (NE, NE)	13.14 (13.14, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.14, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.014 (0.213)
95% CI		(1.986, 4.575)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.3 (83.9, 92.6)	66.9 (62.4, 71.4)
6 months	85.7 (79.3, 92.2)	62.2 (57.1, 67.4)
9 months	85.7 (79.3, 92.2)	59.9 (54.0, 65.8)
12 months	85.7 (79.3, 92.2)	59.9 (54.0, 65.8)
18 months	NE (NE, NE)	44.9 (19.1, 70.7)
Median Follow-up Time (months)	2.79	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	6 (2.7)	86 (19.5)
Number of Subjects Censored, n (%)	215 (97.3)	354 (80.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.11, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.919 (0.423)
95% CI		(3.019, 15.854)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (95.0, 99.4)	82.0 (78.4, 85.7)
6 months	97.2 (95.0, 99.4)	77.9 (73.4, 82.4)
9 months	97.2 (95.0, 99.4)	76.5 (71.3, 81.7)
12 months	97.2 (95.0, 99.4)	76.5 (71.3, 81.7)
18 months	NE (NE, NE)	76.5 (71.3, 81.7)
Median Follow-up Time (months)	2.83	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	8 (3.6)	18 (4.1)
Number of Subjects Censored, n (%)	213 (96.4)	422 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.041 (0.427)
95% CI		(0.451, 2.405)
Log-rank p-value		0.939

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.3 (93.8, 98.8)	95.7 (93.8, 97.7)
6 months	96.3 (93.8, 98.8)	95.7 (93.8, 97.7)
9 months	96.3 (93.8, 98.8)	95.7 (93.8, 97.7)
12 months	96.3 (93.8, 98.8)	95.7 (93.8, 97.7)
18 months	NE (NE, NE)	95.7 (93.8, 97.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	3 (1.4)	13 (3.0)
Number of Subjects Censored, n (%)	218 (98.6)	427 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.915 (0.644)
95% CI		(0.542, 6.770)
Log-rank p-value		0.328

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.0 (97.6, 100.0)	97.1 (95.5, 98.7)
6 months	96.7 (91.9, 100.0)	96.7 (94.9, 98.5)
9 months	96.7 (91.9, 100.0)	96.7 (94.9, 98.5)
12 months	96.7 (91.9, 100.0)	96.7 (94.9, 98.5)
18 months	NE (NE, NE)	96.7 (94.9, 98.5)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Nervous system disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	35 (15.8)	109 (24.8)
Number of Subjects Censored, n (%)	186 (84.2)	331 (75.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.57 (2.56, 11.10)
Median (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.365 (0.196)
95% CI		(0.929, 2.006)
Log-rank p-value		0.132

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Nervous system disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.9 (77.7, 88.1)	78.1 (74.1, 82.0)
6 months	82.9 (77.7, 88.1)	71.8 (66.7, 76.8)
9 months	82.9 (77.7, 88.1)	70.2 (64.8, 75.6)
12 months	82.9 (77.7, 88.1)	66.5 (57.8, 75.2)
18 months	NE (NE, NE)	66.5 (57.8, 75.2)
Median Follow-up Time (months)	2.69	2.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	11 (5.0)	39 (8.9)
Number of Subjects Censored, n (%)	210 (95.0)	401 (91.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
Median (95% CI)	NE (NE, NE)	NE (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.579 (0.345)
95% CI		(0.803, 3.104)
Log-rank p-value		0.186

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.5 (91.2, 97.7)	92.1 (89.6, 94.7)
6 months	94.5 (91.2, 97.7)	91.1 (88.2, 94.0)
9 months	94.5 (91.2, 97.7)	89.5 (85.8, 93.1)
12 months	94.5 (91.2, 97.7)	89.5 (85.8, 93.1)
18 months	NE (NE, NE)	89.5 (85.8, 93.1)
Median Follow-up Time (months)	2.83	3.60

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	6 (2.7)	8 (1.8)
Number of Subjects Censored, n (%)	215 (97.3)	432 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.574 (0.544)
95% CI		(0.197, 1.668)
Log-rank p-value		0.285

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (95.1, 99.4)	98.1 (96.8, 99.4)
6 months	97.2 (95.1, 99.4)	98.1 (96.8, 99.4)
9 months	97.2 (95.1, 99.4)	98.1 (96.8, 99.4)
12 months	97.2 (95.1, 99.4)	98.1 (96.8, 99.4)
18 months	NE (NE, NE)	98.1 (96.8, 99.4)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	4 (1.8)	12 (2.7)
Number of Subjects Censored, n (%)	217 (98.2)	428 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.431 (0.578)
95% CI		(0.461, 4.443)
Log-rank p-value		0.547

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (96.1, 99.9)	97.2 (95.6, 98.8)
6 months	98.0 (96.1, 99.9)	97.2 (95.6, 98.8)
9 months	98.0 (96.1, 99.9)	97.2 (95.6, 98.8)
12 months	98.0 (96.1, 99.9)	97.2 (95.6, 98.8)
18 months	NE (NE, NE)	97.2 (95.6, 98.8)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	29 (13.1)	107 (24.3)
Number of Subjects Censored, n (%)	192 (86.9)	333 (75.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.63 (2.83, 6.93)
Median (95% CI)	NE (NE, NE)	13.60 (11.96, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.549 (0.212)
95% CI		(1.022, 2.347)
Log-rank p-value		0.051

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.0 (81.1, 90.9)	78.6 (74.7, 82.6)
6 months	83.5 (76.8, 90.3)	71.9 (66.8, 77.0)
9 months	83.5 (76.8, 90.3)	69.0 (63.0, 74.9)
12 months	83.5 (76.8, 90.3)	61.3 (46.2, 76.4)
18 months	NE (NE, NE)	46.0 (17.6, 74.3)
Median Follow-up Time (months)	2.76	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	12 (5.4)	75 (17.0)
Number of Subjects Censored, n (%)	209 (94.6)	365 (83.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.60 (6.93, NE)
Median (95% CI)	NE (NE, NE)	NE (13.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.2*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.661 (0.313)
95% CI		(1.441, 4.916)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.2 (91.0, 97.4)	84.4 (80.9, 88.0)
6 months	94.2 (91.0, 97.4)	80.5 (76.1, 84.8)
9 months	94.2 (91.0, 97.4)	77.5 (71.5, 83.4)
12 months	94.2 (91.0, 97.4)	77.5 (71.5, 83.4)
18 months	NE (NE, NE)	58.1 (24.9, 91.3)
Median Follow-up Time (months)	2.79	3.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	5 (2.3)	8 (1.8)
Number of Subjects Censored, n (%)	216 (97.7)	432 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.631 (0.586)
95% CI		(0.200, 1.989)
Log-rank p-value		0.406

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (95.5, 99.7)	98.4 (97.2, 99.6)
6 months	97.6 (95.5, 99.7)	97.9 (96.4, 99.4)
9 months	97.6 (95.5, 99.7)	97.9 (96.4, 99.4)
12 months	97.6 (95.5, 99.7)	97.9 (96.4, 99.4)
18 months	NE (NE, NE)	97.9 (96.4, 99.4)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Infections and infestations**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	28 (12.7)	92 (20.9)
Number of Subjects Censored, n (%)	193 (87.3)	348 (79.1)
Time to first TEAE (months)		
25% percentile (95% CI)	5.78 (4.34, NE)	5.78 (4.63, 7.92)
Median (95% CI)	NE (5.78, NE)	17.48 (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.48, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.176 (0.222)
95% CI		(0.761, 1.817)
Log-rank p-value		0.401

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Infections and infestations**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.2 (83.8, 92.7)	84.4 (80.8, 87.9)
6 months	70.0 (49.6, 90.4)	74.1 (68.6, 79.6)
9 months	70.0 (49.6, 90.4)	65.8 (58.1, 73.6)
12 months	70.0 (49.6, 90.4)	60.8 (48.8, 72.7)
18 months	NE (NE, NE)	45.6 (18.3, 72.9)
Median Follow-up Time (months)	2.79	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	8 (3.6)	18 (4.1)
Number of Subjects Censored, n (%)	213 (96.4)	422 (95.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.724 (0.440)
95% CI		(0.305, 1.716)
Log-rank p-value		0.564

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (96.4, 99.9)	96.9 (95.3, 98.6)
6 months	87.2 (76.4, 97.9)	95.0 (92.3, 97.7)
9 months	87.2 (76.4, 97.9)	93.4 (89.9, 96.9)
12 months	87.2 (76.4, 97.9)	93.4 (89.9, 96.9)
18 months	NE (NE, NE)	93.4 (89.9, 96.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	6 (2.7)	11 (2.5)
Number of Subjects Censored, n (%)	215 (97.3)	429 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.56, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.479 (0.537)
95% CI		(0.167, 1.373)
Log-rank p-value		0.153

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (95.2, 99.7)	99.0 (98.0, 100.0)
6 months	93.8 (86.6, 100.0)	96.5 (94.1, 98.9)
9 months	93.8 (86.6, 100.0)	95.6 (92.6, 98.6)
12 months	93.8 (86.6, 100.0)	90.3 (79.8, 100.0)
18 months	NE (NE, NE)	90.3 (79.8, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	1 (0.5)	11 (2.5)
Number of Subjects Censored, n (%)	220 (99.5)	429 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.221 (1.048)
95% CI		(0.541, 32.944)
Log-rank p-value		0.146

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.6, 100.0)	97.4 (95.8, 99.0)
6 months	99.5 (98.6, 100.0)	96.7 (94.6, 98.8)
9 months	99.5 (98.6, 100.0)	96.7 (94.6, 98.8)
12 months	99.5 (98.6, 100.0)	96.7 (94.6, 98.8)
18 months	NE (NE, NE)	96.7 (94.6, 98.8)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	35 (15.8)	66 (15.0)
Number of Subjects Censored, n (%)	186 (84.2)	374 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.77, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.783 (0.213)
95% CI		(0.516, 1.189)
Log-rank p-value		0.283

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.4 (76.9, 87.8)	86.7 (83.4, 90.0)
6 months	82.4 (76.9, 87.8)	82.5 (78.1, 86.8)
9 months	82.4 (76.9, 87.8)	79.8 (74.6, 84.9)
12 months	82.4 (76.9, 87.8)	79.8 (74.6, 84.9)
18 months	NE (NE, NE)	79.8 (74.6, 84.9)
Median Follow-up Time (months)	2.76	3.45

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	27 (12.2)	36 (8.2)
Number of Subjects Censored, n (%)	194 (87.8)	404 (91.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	17.74 (17.74, NE)
Median (95% CI)	NE (NE, NE)	NE (17.74, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.74, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.479 (0.264)
95% CI		(0.286, 0.804)
Log-rank p-value		0.006

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.0 (81.0, 91.0)	93.9 (91.5, 96.2)
6 months	86.0 (81.0, 91.0)	89.5 (85.8, 93.3)
9 months	86.0 (81.0, 91.0)	88.0 (83.7, 92.3)
12 months	86.0 (81.0, 91.0)	88.0 (83.7, 92.3)
18 months	NE (NE, NE)	58.6 (11.6, 100.0)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	3 (1.4)	29 (6.6)
Number of Subjects Censored, n (%)	218 (98.6)	411 (93.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.860 (0.607)
95% CI		(1.479, 15.968)
Log-rank p-value		0.004

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.9, 100.0)	93.1 (90.6, 95.5)
6 months	98.6 (96.9, 100.0)	93.1 (90.6, 95.5)
9 months	98.6 (96.9, 100.0)	93.1 (90.6, 95.5)
12 months	98.6 (96.9, 100.0)	93.1 (90.6, 95.5)
18 months	NE (NE, NE)	93.1 (90.6, 95.5)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Endocrine disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	1 (0.5)	97 (22.0)
Number of Subjects Censored, n (%)	220 (99.5)	343 (78.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.52 (3.81, 6.01)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		40.424 (1.006)
95% CI		(5.630, 290.239)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Endocrine disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.6, 100.0)	81.8 (78.1, 85.6)
6 months	99.5 (98.6, 100.0)	70.2 (64.3, 76.1)
9 months	99.5 (98.6, 100.0)	67.2 (60.7, 73.8)
12 months	99.5 (98.6, 100.0)	67.2 (60.7, 73.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	1 (0.5)	92 (20.9)
Number of Subjects Censored, n (%)	220 (99.5)	348 (79.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.68 (3.91, 7.33)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		37.470 (1.006)
95% CI		(5.215, 269.241)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.6, 100.0)	83.1 (79.4, 86.8)
6 months	99.5 (98.6, 100.0)	72.1 (66.4, 77.9)
9 months	99.5 (98.6, 100.0)	67.8 (60.9, 74.7)
12 months	99.5 (98.6, 100.0)	67.8 (60.9, 74.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	17 (7.7)	56 (12.7)
Number of Subjects Censored, n (%)	204 (92.3)	384 (87.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.276 (0.280)
95% CI		(0.737, 2.210)
Log-rank p-value		0.387

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.1 (88.4, 95.9)	89.0 (85.8, 92.1)
6 months	90.5 (85.7, 95.3)	83.6 (79.2, 87.9)
9 months	90.5 (85.7, 95.3)	82.6 (78.0, 87.3)
12 months	90.5 (85.7, 95.3)	82.6 (78.0, 87.3)
18 months	NE (NE, NE)	82.6 (78.0, 87.3)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	12 (5.4)	25 (5.7)
Number of Subjects Censored, n (%)	209 (94.6)	415 (94.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.758 (0.356)
95% CI		(0.378, 1.523)
Log-rank p-value		0.438

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.1 (90.9, 97.4)	95.0 (92.7, 97.2)
6 months	94.1 (90.9, 97.4)	92.7 (89.7, 95.6)
9 months	94.1 (90.9, 97.4)	91.7 (88.2, 95.2)
12 months	94.1 (90.9, 97.4)	91.7 (88.2, 95.2)
18 months	NE (NE, NE)	91.7 (88.2, 95.2)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	2 (0.9)	10 (2.3)
Number of Subjects Censored, n (%)	219 (99.1)	430 (97.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.968 (0.781)
95% CI		(0.426, 9.089)
Log-rank p-value		0.437

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.5 (98.5, 100.0)	97.6 (96.1, 99.2)
6 months	97.8 (94.4, 100.0)	97.0 (95.1, 99.0)
9 months	97.8 (94.4, 100.0)	97.0 (95.1, 99.0)
12 months	97.8 (94.4, 100.0)	97.0 (95.1, 99.0)
18 months	NE (NE, NE)	97.0 (95.1, 99.0)
Median Follow-up Time (months)	2.83	3.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	2 (0.9)	11 (2.5)
Number of Subjects Censored, n (%)	219 (99.1)	429 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.221 (0.775)
95% CI		(0.487, 10.133)
Log-rank p-value		0.294

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (97.4, 100.0)	97.8 (96.4, 99.2)
6 months	98.9 (97.4, 100.0)	96.7 (94.7, 98.8)
9 months	98.9 (97.4, 100.0)	96.7 (94.7, 98.8)
12 months	98.9 (97.4, 100.0)	96.7 (94.7, 98.8)
18 months	NE (NE, NE)	96.7 (94.7, 98.8)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	24 (10.9)	50 (11.4)
Number of Subjects Censored, n (%)	197 (89.1)	390 (88.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.66, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.819 (0.253)
95% CI		(0.499, 1.344)
Log-rank p-value		0.463

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.1 (84.9, 93.3)	89.8 (86.9, 92.8)
6 months	87.6 (82.5, 92.7)	86.2 (82.3, 90.1)
9 months	87.6 (82.5, 92.7)	85.0 (80.4, 89.5)
12 months	87.6 (82.5, 92.7)	82.4 (75.7, 89.0)
18 months	NE (NE, NE)	82.4 (75.7, 89.0)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	3 (1.4)	19 (4.3)
Number of Subjects Censored, n (%)	218 (98.6)	421 (95.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.367 (0.627)
95% CI		(0.693, 8.087)
Log-rank p-value		0.172

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.7, 100.0)	95.8 (93.8, 97.9)
6 months	98.5 (96.7, 100.0)	94.7 (92.2, 97.3)
9 months	98.5 (96.7, 100.0)	94.7 (92.2, 97.3)
12 months	98.5 (96.7, 100.0)	91.8 (85.8, 97.9)
18 months	NE (NE, NE)	91.8 (85.8, 97.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Number of Subjects with Events, n (%)	2 (0.9)	14 (3.2)
Number of Subjects Censored, n (%)	219 (99.1)	426 (96.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.601 (0.765)
95% CI		(0.581, 11.649)
Log-rank p-value		0.185

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Yes

Statistics	Placebo + BSC N=221	Fruquintinib + BSC N=440
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.8, 100.0)	97.4 (95.8, 98.9)
6 months	99.1 (97.8, 100.0)	96.2 (94.0, 98.4)
9 months	99.1 (97.8, 100.0)	94.9 (91.6, 98.3)
12 months	99.1 (97.8, 100.0)	94.9 (91.6, 98.3)
18 months	NE (NE, NE)	94.9 (91.6, 98.3)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	5 (55.6)	11 (68.8)
Number of Subjects Censored, n (%)	4 (44.4)	5 (31.3)
Time to first TEAE (months)		
25% percentile (95% CI)	1.22 (0.23, 1.64)	0.11 (0.03, 1.51)
Median (95% CI)	1.64 (0.23, NE)	2.53 (0.07, 6.97)
75% percentile (95% CI)	NE (1.35, NE)	6.97 (1.51, NE)
Min, Max	0.2, 4.7*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.592 (0.840)
95% CI		(0.114, 3.068)
Log-rank p-value		0.647

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	44.4 (12.0, 76.9)	50.0 (25.5, 74.5)
6 months	NE (NE, NE)	31.3 (5.3, 57.2)
9 months	NE (NE, NE)	15.6 (0.0, 40.9)
12 months	NE (NE, NE)	15.6 (0.0, 40.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.64	2.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	1 (11.1)	4 (25.0)
Number of Subjects Censored, n (%)	8 (88.9)	12 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.35, NE)	NE (0.03, NE)
Median (95% CI)	NE (1.35, NE)	NE (0.99, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.000 (1.414)
95% CI		(0.063, 15.988)
Log-rank p-value		1.000

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (64.6, 100.0)	75.0 (53.8, 96.2)
6 months	NE (NE, NE)	75.0 (53.8, 96.2)
9 months	NE (NE, NE)	75.0 (53.8, 96.2)
12 months	NE (NE, NE)	75.0 (53.8, 96.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	3 (33.3)	3 (18.8)
Number of Subjects Censored, n (%)	6 (66.7)	13 (81.3)
Time to first TEAE (months)		
25% percentile (95% CI)	1.64 (0.23, NE)	6.97 (0.07, NE)
Median (95% CI)	NE (0.23, NE)	NE (6.97, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 4.7*	0.1, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.206 (1.316)
95% CI		(0.016, 2.715)
Log-rank p-value		0.433

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	64.8 (32.4, 97.2)	87.5 (71.3, 100.0)
6 months	NE (NE, NE)	87.5 (71.3, 100.0)
9 months	NE (NE, NE)	72.9 (43.5, 100.0)
12 months	NE (NE, NE)	72.9 (43.5, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.39

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	3 (18.8)
Number of Subjects Censored, n (%)	9 (100.0)	13 (81.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.10, NE)
Median (95% CI)	NE (NE, NE)	NE (3.55, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	0.1, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	87.5 (71.3, 100.0)
6 months	NE (NE, NE)	79.5 (58.6, 100.0)
9 months	NE (NE, NE)	79.5 (58.6, 100.0)
12 months	NE (NE, NE)	79.5 (58.6, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	5 (31.3)
Number of Subjects Censored, n (%)	9 (100.0)	11 (68.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	2.46 (0.07, NE)
Median (95% CI)	NE (NE, NE)	NE (2.46, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	0.1, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	74.5 (52.8, 96.1)
6 months	NE (NE, NE)	63.8 (37.1, 90.6)
9 months	NE (NE, NE)	63.8 (37.1, 90.6)
12 months	NE (NE, NE)	63.8 (37.1, 90.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	3.37

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	1 (11.1)	0
Number of Subjects Censored, n (%)	8 (88.9)	16 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.22, NE)	NE (NE, NE)
Median (95% CI)	NE (1.22, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2, 4.7*	1.7*, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (68.4, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	5.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	1 (6.3)
Number of Subjects Censored, n (%)	9 (100.0)	15 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.61, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	1.7*, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	90.9 (73.9, 100.0)
9 months	NE (NE, NE)	90.9 (73.9, 100.0)
12 months	NE (NE, NE)	90.9 (73.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	5.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	4 (44.4)	14 (87.5)
Number of Subjects Censored, n (%)	5 (55.6)	2 (12.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.07, NE)	0.07 (0.03, 1.51)
Median (95% CI)	NE (0.07, NE)	1.56 (0.07, 2.46)
75% percentile (95% CI)	NE (0.69, NE)	3.02 (1.51, NE)
Min, Max	0.1, 4.7*	0.0, 3.7
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.603 (0.912)
95% CI		(0.436, 15.538)
Log-rank p-value		0.446

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	55.6 (23.1, 88.0)	25.0 (3.8, 46.2)
6 months	NE (NE, NE)	0.0 (NE, NE)
9 months	NE (NE, NE)	0.0 (NE, NE)
12 months	NE (NE, NE)	0.0 (NE, NE)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	1.22	1.56

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	2 (22.2)	5 (31.3)
Number of Subjects Censored, n (%)	7 (77.8)	11 (68.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.07, NE)	3.71 (0.07, NE)
Median (95% CI)	NE (0.07, NE)	NE (3.71, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (5.95, NE)
Min, Max	0.1, 4.7*	0.1, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.852 (1.292)
95% CI		(0.147, 23.285)
Log-rank p-value		0.433

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.8 (50.6, 100.0)	80.8 (61.2, 100.0)
6 months	NE (NE, NE)	53.8 (18.4, 89.3)
9 months	NE (NE, NE)	53.8 (18.4, 89.3)
12 months	NE (NE, NE)	53.8 (18.4, 89.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	1 (11.1)	4 (25.0)
Number of Subjects Censored, n (%)	8 (88.9)	12 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	9.20 (0.03, NE)
Median (95% CI)	NE (0.69, NE)	NE (4.21, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (9.20, NE)
Min, Max	0.7, 4.7*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.324 (1.653)
95% CI		(0.013, 8.276)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (68.4, 100.0)	93.8 (81.9, 100.0)
6 months	NE (NE, NE)	75.8 (51.3, 100.0)
9 months	NE (NE, NE)	75.8 (51.3, 100.0)
12 months	NE (NE, NE)	60.6 (27.6, 93.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.42

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	1 (11.1)	3 (18.8)
Number of Subjects Censored, n (%)	8 (88.9)	13 (81.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	9.23 (1.51, NE)
Median (95% CI)	NE (0.95, NE)	NE (4.21, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (9.23, NE)
Min, Max	1.0, 4.7*	1.5, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.067 (>999)
95% CI		(0.000, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (68.4, 100.0)	93.8 (81.9, 100.0)
6 months	NE (NE, NE)	84.4 (63.9, 100.0)
9 months	NE (NE, NE)	84.4 (63.9, 100.0)
12 months	NE (NE, NE)	67.5 (33.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.85

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	1 (6.3)
Number of Subjects Censored, n (%)	9 (100.0)	15 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.46, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	1.7*, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.3 (80.7, 100.0)
6 months	NE (NE, NE)	93.3 (80.7, 100.0)
9 months	NE (NE, NE)	93.3 (80.7, 100.0)
12 months	NE (NE, NE)	93.3 (80.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	2 (22.2)	3 (18.8)
Number of Subjects Censored, n (%)	7 (77.8)	13 (81.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	9.20 (0.07, NE)
Median (95% CI)	NE (0.69, NE)	NE (4.21, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (9.20, NE)
Min, Max	0.7, 4.7*	0.1, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.000 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.090

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.2 (47.2, 100.0)	93.8 (81.9, 100.0)
6 months	NE (NE, NE)	84.4 (63.9, 100.0)
9 months	NE (NE, NE)	84.4 (63.9, 100.0)
12 months	NE (NE, NE)	67.5 (33.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.85

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	4 (25.0)
Number of Subjects Censored, n (%)	9 (100.0)	12 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.53 (0.07, NE)
Median (95% CI)	NE (NE, NE)	NE (4.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	0.1, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	81.3 (62.1, 100.0)
6 months	NE (NE, NE)	69.6 (43.0, 96.3)
9 months	NE (NE, NE)	69.6 (43.0, 96.3)
12 months	NE (NE, NE)	69.6 (43.0, 96.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	2 (12.5)
Number of Subjects Censored, n (%)	9 (100.0)	14 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.71, NE)
Median (95% CI)	NE (NE, NE)	NE (5.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	1.7, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.480

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.8 (81.9, 100.0)
6 months	NE (NE, NE)	80.4 (54.0, 100.0)
9 months	NE (NE, NE)	80.4 (54.0, 100.0)
12 months	NE (NE, NE)	80.4 (54.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	5.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	1 (11.1)	0
Number of Subjects Censored, n (%)	8 (88.9)	16 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.30, NE)	NE (NE, NE)
Median (95% CI)	NE (0.30, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 4.7*	1.7*, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (68.4, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	5.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	2 (12.5)
Number of Subjects Censored, n (%)	9 (100.0)	14 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.07, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	0.1, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	87.5 (71.3, 100.0)
6 months	NE (NE, NE)	87.5 (71.3, 100.0)
9 months	NE (NE, NE)	87.5 (71.3, 100.0)
12 months	NE (NE, NE)	87.5 (71.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	5.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	4 (44.4)	6 (37.5)
Number of Subjects Censored, n (%)	5 (55.6)	10 (62.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.23, NE)	2.37 (0.03, NE)
Median (95% CI)	NE (0.23, NE)	NE (1.15, NE)
75% percentile (95% CI)	NE (1.35, NE)	NE (5.68, NE)
Min, Max	0.2, 4.7*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.369 (0.957)
95% CI		(0.057, 2.407)
Log-rank p-value		0.237

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	55.6 (23.1, 88.0)	75.0 (53.8, 96.2)
6 months	NE (NE, NE)	53.3 (22.9, 83.8)
9 months	NE (NE, NE)	53.3 (22.9, 83.8)
12 months	NE (NE, NE)	53.3 (22.9, 83.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	1 (11.1)	4 (25.0)
Number of Subjects Censored, n (%)	8 (88.9)	12 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.23, NE)	6.97 (0.03, NE)
Median (95% CI)	NE (0.23, NE)	NE (3.58, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 4.7*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.441 (1.564)
95% CI		(0.021, 9.464)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (68.4, 100.0)	87.5 (71.3, 100.0)
6 months	NE (NE, NE)	78.8 (56.9, 100.0)
9 months	NE (NE, NE)	65.6 (35.9, 95.3)
12 months	NE (NE, NE)	65.6 (35.9, 95.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.11

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	1 (6.3)
Number of Subjects Censored, n (%)	9 (100.0)	15 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.15, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	1.1, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.8 (81.9, 100.0)
6 months	NE (NE, NE)	93.8 (81.9, 100.0)
9 months	NE (NE, NE)	93.8 (81.9, 100.0)
12 months	NE (NE, NE)	93.8 (81.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	5.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	2 (12.5)
Number of Subjects Censored, n (%)	9 (100.0)	14 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.65, NE)
Median (95% CI)	NE (NE, NE)	NE (5.68, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	1.7*, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	75.8 (45.2, 100.0)
9 months	NE (NE, NE)	75.8 (45.2, 100.0)
12 months	NE (NE, NE)	75.8 (45.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	1 (11.1)	0
Number of Subjects Censored, n (%)	8 (88.9)	16 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.35, NE)	NE (NE, NE)
Median (95% CI)	NE (1.35, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	1.7*, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (64.6, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	5.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	1 (11.1)	0
Number of Subjects Censored, n (%)	8 (88.9)	16 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (NE, NE)
Median (95% CI)	NE (0.95, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 4.7*	1.7*, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (68.4, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	5.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	3 (33.3)	5 (31.3)
Number of Subjects Censored, n (%)	6 (66.7)	11 (68.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.46, NE)	3.56 (0.69, NE)
Median (95% CI)	NE (0.46, NE)	NE (2.46, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 4.7*	0.7, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.333 (1.242)
95% CI		(0.029, 3.796)
Log-rank p-value		0.433

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	66.7 (35.9, 97.5)	75.0 (53.8, 96.2)
6 months	NE (NE, NE)	64.3 (37.7, 90.9)
9 months	NE (NE, NE)	64.3 (37.7, 90.9)
12 months	NE (NE, NE)	64.3 (37.7, 90.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	1 (6.3)
Number of Subjects Censored, n (%)	9 (100.0)	15 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	0.7, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.8 (81.9, 100.0)
6 months	NE (NE, NE)	93.8 (81.9, 100.0)
9 months	NE (NE, NE)	93.8 (81.9, 100.0)
12 months	NE (NE, NE)	93.8 (81.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	5.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	1 (6.3)
Number of Subjects Censored, n (%)	9 (100.0)	15 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	0.7, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.8 (81.9, 100.0)
6 months	NE (NE, NE)	93.8 (81.9, 100.0)
9 months	NE (NE, NE)	93.8 (81.9, 100.0)
12 months	NE (NE, NE)	93.8 (81.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	5.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	2 (12.5)
Number of Subjects Censored, n (%)	9 (100.0)	14 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.64, NE)
Median (95% CI)	NE (NE, NE)	NE (6.37, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	1.6, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.8 (81.9, 100.0)
6 months	NE (NE, NE)	93.8 (81.9, 100.0)
9 months	NE (NE, NE)	78.1 (48.5, 100.0)
12 months	NE (NE, NE)	78.1 (48.5, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	1 (11.1)	0
Number of Subjects Censored, n (%)	8 (88.9)	16 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.87, NE)	NE (NE, NE)
Median (95% CI)	NE (1.87, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	1.7*, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (64.6, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	5.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	1 (6.3)
Number of Subjects Censored, n (%)	9 (100.0)	15 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.67, NE)
Median (95% CI)	NE (NE, NE)	NE (4.67, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	1.7*, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	88.9 (68.4, 100.0)
9 months	NE (NE, NE)	88.9 (68.4, 100.0)
12 months	NE (NE, NE)	88.9 (68.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.85

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	1 (11.1)	5 (31.3)
Number of Subjects Censored, n (%)	8 (88.9)	11 (68.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.76, NE)	5.52 (0.10, NE)
Median (95% CI)	NE (0.76, NE)	7.56 (5.52, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (7.56, NE)
Min, Max	0.8, 4.7*	0.1, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.228 (1.673)
95% CI		(0.009, 6.051)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (68.4, 100.0)	80.8 (61.2, 100.0)
6 months	NE (NE, NE)	64.6 (32.2, 97.0)
9 months	NE (NE, NE)	48.5 (11.8, 85.1)
12 months	NE (NE, NE)	48.5 (11.8, 85.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.19

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	1 (6.3)
Number of Subjects Censored, n (%)	9 (100.0)	15 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.46, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	0.5, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.8 (81.9, 100.0)
6 months	NE (NE, NE)	93.8 (81.9, 100.0)
9 months	NE (NE, NE)	93.8 (81.9, 100.0)
12 months	NE (NE, NE)	93.8 (81.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	1 (11.1)	2 (12.5)
Number of Subjects Censored, n (%)	8 (88.9)	14 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.76, NE)	10.28 (5.52, NE)
Median (95% CI)	NE (0.76, NE)	NE (5.52, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (10.28, NE)
Min, Max	0.8, 4.7*	1.7*, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.000 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (68.4, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	85.7 (59.8, 100.0)
9 months	NE (NE, NE)	85.7 (59.8, 100.0)
12 months	NE (NE, NE)	57.1 (8.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	5.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	1 (6.3)
Number of Subjects Censored, n (%)	9 (100.0)	15 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.10, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	0.1, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.8 (81.9, 100.0)
6 months	NE (NE, NE)	93.8 (81.9, 100.0)
9 months	NE (NE, NE)	93.8 (81.9, 100.0)
12 months	NE (NE, NE)	93.8 (81.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	1 (6.3)
Number of Subjects Censored, n (%)	9 (100.0)	15 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.50, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	1.7*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.3 (80.7, 100.0)
6 months	NE (NE, NE)	93.3 (80.7, 100.0)
9 months	NE (NE, NE)	93.3 (80.7, 100.0)
12 months	NE (NE, NE)	93.3 (80.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Vascular disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	2 (22.2)	8 (50.0)
Number of Subjects Censored, n (%)	7 (77.8)	8 (50.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.46, NE)	0.18 (0.07, 2.79)
Median (95% CI)	NE (0.46, NE)	2.79 (0.16, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (2.79, NE)
Min, Max	0.5, 4.7*	0.1, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		7.021 (1.313)
95% CI		(0.535, 92.126)
Log-rank p-value		0.090

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Vascular disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.8 (50.6, 100.0)	49.2 (24.3, 74.1)
6 months	NE (NE, NE)	49.2 (24.3, 74.1)
9 months	NE (NE, NE)	49.2 (24.3, 74.1)
12 months	NE (NE, NE)	49.2 (24.3, 74.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	1 (11.1)	8 (50.0)
Number of Subjects Censored, n (%)	8 (88.9)	8 (50.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.41, NE)	0.39 (0.07, 2.79)
Median (95% CI)	NE (1.41, NE)	2.79 (0.16, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (2.79, NE)
Min, Max	1.2*, 4.7*	0.1, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		>999 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.090

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (64.6, 100.0)	49.2 (24.3, 74.1)
6 months	NE (NE, NE)	49.2 (24.3, 74.1)
9 months	NE (NE, NE)	49.2 (24.3, 74.1)
12 months	NE (NE, NE)	49.2 (24.3, 74.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	1 (11.1)	7 (43.8)
Number of Subjects Censored, n (%)	8 (88.9)	9 (56.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	0.69 (0.03, 7.66)
Median (95% CI)	NE (0.03, NE)	7.66 (0.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (7.66, NE)
Min, Max	0.0, 4.7*	0.0, 8.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		>999 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (68.4, 100.0)	68.8 (46.0, 91.5)
6 months	NE (NE, NE)	60.2 (34.8, 85.5)
9 months	NE (NE, NE)	NE (NE, NE)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	2 (12.5)
Number of Subjects Censored, n (%)	9 (100.0)	14 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.03, NE)
Median (95% CI)	NE (NE, NE)	NE (3.71, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.8 (81.9, 100.0)
6 months	NE (NE, NE)	84.4 (63.9, 100.0)
9 months	NE (NE, NE)	84.4 (63.9, 100.0)
12 months	NE (NE, NE)	84.4 (63.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.19

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	2 (12.5)
Number of Subjects Censored, n (%)	9 (100.0)	14 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.39, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	0.4, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	87.5 (71.3, 100.0)
6 months	NE (NE, NE)	87.5 (71.3, 100.0)
9 months	NE (NE, NE)	87.5 (71.3, 100.0)
12 months	NE (NE, NE)	87.5 (71.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.19

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	1 (6.3)
Number of Subjects Censored, n (%)	9 (100.0)	15 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.52, NE)
Median (95% CI)	NE (NE, NE)	NE (5.52, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	1.7*, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	85.7 (59.8, 100.0)
9 months	NE (NE, NE)	85.7 (59.8, 100.0)
12 months	NE (NE, NE)	85.7 (59.8, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	5.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	1 (11.1)	4 (25.0)
Number of Subjects Censored, n (%)	8 (88.9)	12 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.07, NE)	4.86 (0.62, NE)
Median (95% CI)	NE (0.07, NE)	NE (4.86, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 4.7*	0.6, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.608 (>999)
95% CI		(0.000, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (68.4, 100.0)	80.8 (61.2, 100.0)
6 months	NE (NE, NE)	69.2 (42.4, 96.1)
9 months	NE (NE, NE)	69.2 (42.4, 96.1)
12 months	NE (NE, NE)	69.2 (42.4, 96.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.19

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	2 (12.5)
Number of Subjects Censored, n (%)	9 (100.0)	14 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.50, NE)
Median (95% CI)	NE (NE, NE)	NE (4.86, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	1.7*, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.3 (80.7, 100.0)
6 months	NE (NE, NE)	81.7 (57.6, 100.0)
9 months	NE (NE, NE)	81.7 (57.6, 100.0)
12 months	NE (NE, NE)	81.7 (57.6, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Nervous system disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	2 (22.2)	6 (37.5)
Number of Subjects Censored, n (%)	7 (77.8)	10 (62.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.92, NE)	0.79 (0.07, NE)
Median (95% CI)	NE (0.92, NE)	NE (0.46, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9, 4.7*	0.1, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.750 (0.979)
95% CI		(0.257, 11.924)
Log-rank p-value		0.763

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Nervous system disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.2 (47.2, 100.0)	62.5 (38.8, 86.2)
6 months	NE (NE, NE)	62.5 (38.8, 86.2)
9 months	NE (NE, NE)	62.5 (38.8, 86.2)
12 months	NE (NE, NE)	62.5 (38.8, 86.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	2 (12.5)
Number of Subjects Censored, n (%)	9 (100.0)	14 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.07, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	0.1, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	87.5 (71.3, 100.0)
6 months	NE (NE, NE)	87.5 (71.3, 100.0)
9 months	NE (NE, NE)	87.5 (71.3, 100.0)
12 months	NE (NE, NE)	87.5 (71.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	5.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	1 (11.1)	2 (12.5)
Number of Subjects Censored, n (%)	8 (88.9)	14 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.92, NE)	NE (0.39, NE)
Median (95% CI)	NE (0.92, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9, 4.7*	0.4, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.000 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (68.4, 100.0)	87.1 (70.3, 100.0)
6 months	NE (NE, NE)	87.1 (70.3, 100.0)
9 months	NE (NE, NE)	87.1 (70.3, 100.0)
12 months	NE (NE, NE)	87.1 (70.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.19

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	1 (11.1)	5 (31.3)
Number of Subjects Censored, n (%)	8 (88.9)	11 (68.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.35, NE)	3.61 (0.69, NE)
Median (95% CI)	NE (1.35, NE)	NE (3.61, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	0.7, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.000 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (64.6, 100.0)	80.8 (61.2, 100.0)
6 months	NE (NE, NE)	62.8 (36.1, 89.5)
9 months	NE (NE, NE)	62.8 (36.1, 89.5)
12 months	NE (NE, NE)	62.8 (36.1, 89.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	3.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	4 (25.0)
Number of Subjects Censored, n (%)	9 (100.0)	12 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	3.71 (1.15, NE)
Median (95% CI)	NE (NE, NE)	NE (3.61, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	1.1, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	87.1 (70.3, 100.0)
6 months	NE (NE, NE)	69.6 (44.2, 95.1)
9 months	NE (NE, NE)	69.6 (44.2, 95.1)
12 months	NE (NE, NE)	69.6 (44.2, 95.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	2 (12.5)
Number of Subjects Censored, n (%)	9 (100.0)	14 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	0.7, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	87.5 (71.3, 100.0)
6 months	NE (NE, NE)	87.5 (71.3, 100.0)
9 months	NE (NE, NE)	87.5 (71.3, 100.0)
12 months	NE (NE, NE)	87.5 (71.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Infections and infestations**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	1 (11.1)	4 (25.0)
Number of Subjects Censored, n (%)	8 (88.9)	12 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.46, NE)	6.83 (0.36, NE)
Median (95% CI)	NE (0.46, NE)	NE (6.83, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 4.7*	0.4, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.000 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Infections and infestations**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (68.4, 100.0)	87.1 (70.3, 100.0)
6 months	NE (NE, NE)	87.1 (70.3, 100.0)
9 months	NE (NE, NE)	62.2 (30.7, 93.7)
12 months	NE (NE, NE)	62.2 (30.7, 93.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.19

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	1 (6.3)
Number of Subjects Censored, n (%)	9 (100.0)	15 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.93, NE)
Median (95% CI)	NE (NE, NE)	NE (6.93, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	1.7*, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	85.7 (59.8, 100.0)
12 months	NE (NE, NE)	85.7 (59.8, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	5.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	1 (6.3)
Number of Subjects Censored, n (%)	9 (100.0)	15 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	1.7*, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.3 (80.7, 100.0)
6 months	NE (NE, NE)	93.3 (80.7, 100.0)
9 months	NE (NE, NE)	93.3 (80.7, 100.0)
12 months	NE (NE, NE)	93.3 (80.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.85

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	2 (22.2)	1 (6.3)
Number of Subjects Censored, n (%)	7 (77.8)	15 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.46, NE)	NE (0.99, NE)
Median (95% CI)	NE (0.46, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 4.7*	1.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.000 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.090

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.8 (50.6, 100.0)	93.8 (81.9, 100.0)
6 months	NE (NE, NE)	93.8 (81.9, 100.0)
9 months	NE (NE, NE)	93.8 (81.9, 100.0)
12 months	NE (NE, NE)	93.8 (81.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	1 (11.1)	0
Number of Subjects Censored, n (%)	8 (88.9)	16 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (NE, NE)
Median (95% CI)	NE (0.95, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 4.7*	1.7*, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.317

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (68.4, 100.0)	100.0 (100.0, 100.0)
6 months	NE (NE, NE)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	5.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	1 (6.3)
Number of Subjects Censored, n (%)	9 (100.0)	15 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.99, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	1.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.8 (81.9, 100.0)
6 months	NE (NE, NE)	93.8 (81.9, 100.0)
9 months	NE (NE, NE)	93.8 (81.9, 100.0)
12 months	NE (NE, NE)	93.8 (81.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Endocrine disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	3 (18.8)
Number of Subjects Censored, n (%)	9 (100.0)	13 (81.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	9.33 (1.15, NE)
Median (95% CI)	NE (NE, NE)	NE (9.33, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (9.33, NE)
Min, Max	1.2*, 4.7*	1.1, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Endocrine disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	87.5 (71.3, 100.0)
6 months	NE (NE, NE)	87.5 (71.3, 100.0)
9 months	NE (NE, NE)	87.5 (71.3, 100.0)
12 months	NE (NE, NE)	65.6 (26.6, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	2 (12.5)
Number of Subjects Censored, n (%)	9 (100.0)	14 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	9.33 (1.91, NE)
Median (95% CI)	NE (NE, NE)	NE (9.33, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (9.33, NE)
Min, Max	1.2*, 4.7*	1.7*, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.3 (80.7, 100.0)
6 months	NE (NE, NE)	93.3 (80.7, 100.0)
9 months	NE (NE, NE)	93.3 (80.7, 100.0)
12 months	NE (NE, NE)	70.0 (29.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Psychiatric disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	2 (12.5)
Number of Subjects Censored, n (%)	9 (100.0)	14 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.03, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Psychiatric disorders**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	87.5 (71.3, 100.0)
6 months	NE (NE, NE)	87.5 (71.3, 100.0)
9 months	NE (NE, NE)	87.5 (71.3, 100.0)
12 months	NE (NE, NE)	87.5 (71.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	1 (6.3)
Number of Subjects Censored, n (%)	9 (100.0)	15 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.95, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	1.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.8 (81.9, 100.0)
6 months	NE (NE, NE)	93.8 (81.9, 100.0)
9 months	NE (NE, NE)	93.8 (81.9, 100.0)
12 months	NE (NE, NE)	93.8 (81.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	5.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3L
Summary of Time to Onset of TEAE by SOC/PT by Prior VEGFi
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
No

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Number of Subjects with Events, n (%)	0	1 (6.3)
Number of Subjects Censored, n (%)	9 (100.0)	15 (93.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (0.03, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.2*, 4.7*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		NE

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=9	Fruquintinib + BSC N=16
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.8 (81.9, 100.0)
6 months	NE (NE, NE)	93.8 (81.9, 100.0)
9 months	NE (NE, NE)	93.8 (81.9, 100.0)
12 months	NE (NE, NE)	93.8 (81.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.83

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	54 (61.4)	130 (72.6)
Number of Subjects Censored, n (%)	34 (38.6)	49 (27.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.49 (0.16, 0.72)	0.30 (0.16, 0.46)
Median (95% CI)	1.84 (0.95, 3.19)	0.99 (0.69, 1.84)
75% percentile (95% CI)	NE (3.71, NE)	5.59 (3.71, 7.29)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Min, Max	0.0, 6.8*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.131 (0.165)
95% CI		(0.819, 1.562)
Log-rank p-value		0.488

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	40.2 (29.6, 50.8)	37.3 (30.1, 44.5)
6 months	26.9 (11.6, 42.2)	23.8 (16.4, 31.3)
9 months	NE (NE, NE)	13.4 (5.3, 21.6)
12 months	NE (NE, NE)	13.4 (5.3, 21.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.46	0.99

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	23 (26.1)	67 (37.4)
Number of Subjects Censored, n (%)	65 (73.9)	112 (62.6)
Time to first TEAE (months)		
25% percentile (95% CI)	2.60 (0.72, NE)	1.18 (0.69, 1.87)
Median (95% CI)	NE (4.70, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.353 (0.244)
95% CI		(0.838, 2.184)
Log-rank p-value		0.235

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.9 (64.4, 83.4)	63.8 (56.6, 71.0)
6 months	63.3 (42.5, 84.1)	60.8 (53.2, 68.5)
9 months	NE (NE, NE)	59.1 (51.0, 67.2)
12 months	NE (NE, NE)	59.1 (51.0, 67.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	15 (17.0)	37 (20.7)
Number of Subjects Censored, n (%)	73 (83.0)	142 (79.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.87, NE)	7.29 (3.32, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.111 (0.311)
95% CI		(0.603, 2.045)
Log-rank p-value		0.810

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.9 (73.5, 90.3)	82.3 (76.6, 88.0)
6 months	81.9 (73.5, 90.3)	78.2 (71.6, 84.9)
9 months	NE (NE, NE)	73.2 (64.1, 82.4)
12 months	NE (NE, NE)	73.2 (64.1, 82.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	11 (12.5)	26 (14.5)
Number of Subjects Censored, n (%)	77 (87.5)	153 (85.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.70, NE)	NE (6.41, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.965 (0.369)
95% CI		(0.469, 1.988)
Log-rank p-value		0.864

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.7 (80.5, 94.9)	88.5 (83.8, 93.3)
6 months	77.9 (58.8, 97.0)	83.5 (77.4, 89.7)
9 months	NE (NE, NE)	81.9 (75.0, 88.7)
12 months	NE (NE, NE)	81.9 (75.0, 88.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	23 (12.8)
Number of Subjects Censored, n (%)	87 (98.9)	156 (87.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.26, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		9.510 (1.025)
95% CI		(1.275, 70.907)
Log-rank p-value		0.007

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.6, 100.0)	88.5 (83.8, 93.3)
6 months	98.9 (96.6, 100.0)	86.6 (81.2, 91.9)
9 months	NE (NE, NE)	83.4 (75.4, 91.4)
12 months	NE (NE, NE)	83.4 (75.4, 91.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	11 (12.5)	11 (6.1)
Number of Subjects Censored, n (%)	77 (87.5)	168 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.19, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.298 (0.446)
95% CI		(0.124, 0.716)
Log-rank p-value		0.005

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.0 (80.6, 95.5)	95.7 (92.7, 98.8)
6 months	79.6 (66.5, 92.8)	91.6 (86.6, 96.6)
9 months	NE (NE, NE)	91.6 (86.6, 96.6)
12 months	NE (NE, NE)	91.6 (86.6, 96.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	5 (5.7)	7 (3.9)
Number of Subjects Censored, n (%)	83 (94.3)	172 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.97, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.479 (0.621)
95% CI		(0.142, 1.619)
Log-rank p-value		0.196

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.2 (89.2, 99.1)	96.5 (93.7, 99.3)
6 months	94.2 (89.2, 99.1)	96.5 (93.7, 99.3)
9 months	NE (NE, NE)	91.4 (81.4, 100.0)
12 months	NE (NE, NE)	91.4 (81.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	11 (6.1)
Number of Subjects Censored, n (%)	87 (98.9)	168 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.00, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.3, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.336 (1.082)
95% CI		(0.280, 19.491)
Log-rank p-value		0.535

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.6, 100.0)	97.7 (95.4, 99.9)
6 months	98.8 (96.6, 100.0)	93.6 (89.0, 98.1)
9 months	NE (NE, NE)	90.5 (83.2, 97.8)
12 months	NE (NE, NE)	78.4 (61.2, 95.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	6 (3.4)
Number of Subjects Censored, n (%)	87 (98.9)	173 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.966 (1.112)
95% CI		(0.222, 17.388)
Log-rank p-value		0.591

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (94.1, 100.0)	96.9 (94.1, 99.6)
6 months	98.0 (94.1, 100.0)	96.9 (94.1, 99.6)
9 months	NE (NE, NE)	93.6 (86.9, 100.0)
12 months	NE (NE, NE)	93.6 (86.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	4 (2.2)
Number of Subjects Censored, n (%)	88 (100.0)	175 (97.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.189

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.3 (96.4, 100.0)
6 months	100.0 (100.0, 100.0)	97.3 (94.7, 100.0)
9 months	NE (NE, NE)	97.3 (94.7, 100.0)
12 months	NE (NE, NE)	97.3 (94.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	58 (65.9)	119 (66.5)
Number of Subjects Censored, n (%)	30 (34.1)	60 (33.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.39 (0.07, 0.66)	0.49 (0.26, 0.69)
Median (95% CI)	1.31 (0.72, 1.84)	1.58 (0.95, 2.40)
75% percentile (95% CI)	3.75 (2.07, NE)	7.79 (4.40, NE)
Min, Max	0.0, 5.6*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.855 (0.164)
95% CI		(0.620, 1.180)
Log-rank p-value		0.303

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	32.1 (21.1, 43.0)	38.6 (31.3, 46.0)
6 months	NE (NE, NE)	28.8 (20.7, 36.9)
9 months	NE (NE, NE)	22.4 (12.3, 32.4)
12 months	NE (NE, NE)	14.9 (1.2, 28.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.02	1.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	9 (10.2)	45 (25.1)
Number of Subjects Censored, n (%)	79 (89.8)	134 (74.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.39 (1.87, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.177 (0.370)
95% CI		(1.055, 4.493)
Log-rank p-value		0.035

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.5 (83.1, 96.0)	78.1 (71.9, 84.3)
6 months	89.5 (83.1, 96.0)	70.3 (61.7, 79.0)
9 months	NE (NE, NE)	66.5 (56.8, 76.2)
12 months	NE (NE, NE)	66.5 (56.8, 76.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	18 (20.5)	33 (18.4)
Number of Subjects Censored, n (%)	70 (79.5)	146 (81.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.92, NE)	9.00 (4.63, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.682 (0.304)
95% CI		(0.376, 1.237)
Log-rank p-value		0.231

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.9 (70.2, 87.6)	84.5 (78.9, 90.0)
6 months	78.9 (70.2, 87.6)	81.4 (75.0, 87.7)
9 months	NE (NE, NE)	77.7 (69.8, 85.6)
12 months	NE (NE, NE)	67.6 (52.9, 82.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.73	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	18 (20.5)	31 (17.3)
Number of Subjects Censored, n (%)	70 (79.5)	148 (82.7)
Time to first TEAE (months)		
25% percentile (95% CI)	4.57 (1.45, NE)	9.23 (6.41, NE)
Median (95% CI)	NE (4.57, NE)	NE (10.12, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.597 (0.313)
95% CI		(0.323, 1.104)
Log-rank p-value		0.103

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.9 (68.0, 87.8)	87.1 (82.1, 92.2)
6 months	69.2 (51.0, 87.5)	83.3 (77.3, 89.4)
9 months	NE (NE, NE)	75.3 (64.8, 85.8)
12 months	NE (NE, NE)	60.8 (40.4, 81.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.52

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	14 (15.9)	34 (19.0)
Number of Subjects Censored, n (%)	74 (84.1)	145 (81.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.92, NE)	NE (3.75, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.951 (0.324)
95% CI		(0.504, 1.795)
Log-rank p-value		0.831

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.2 (72.6, 91.8)	83.4 (77.8, 89.1)
6 months	78.8 (67.4, 90.1)	75.7 (67.7, 83.7)
9 months	NE (NE, NE)	75.7 (67.7, 83.7)
12 months	NE (NE, NE)	75.7 (67.7, 83.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	11 (12.5)	29 (16.2)
Number of Subjects Censored, n (%)	77 (87.5)	150 (83.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.52, NE)	9.20 (6.21, NE)
Median (95% CI)	NE (NE, NE)	NE (10.18, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.967 (0.367)
95% CI		(0.471, 1.986)
Log-rank p-value		0.934

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.7 (80.5, 94.9)	87.7 (82.8, 92.7)
6 months	82.8 (71.3, 94.3)	84.4 (78.3, 90.5)
9 months	NE (NE, NE)	78.5 (69.8, 87.2)
12 months	NE (NE, NE)	65.6 (47.5, 83.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	7 (8.0)	29 (16.2)
Number of Subjects Censored, n (%)	81 (92.0)	150 (83.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.98, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.086 (0.425)
95% CI		(0.907, 4.801)
Log-rank p-value		0.072

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.5 (85.4, 97.5)	85.4 (80.2, 90.6)
6 months	91.5 (85.4, 97.5)	83.3 (77.4, 89.1)
9 months	NE (NE, NE)	80.1 (71.7, 88.4)
12 months	NE (NE, NE)	80.1 (71.7, 88.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	2 (2.3)	11 (6.1)
Number of Subjects Censored, n (%)	86 (97.7)	168 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.423 (0.780)
95% CI		(0.526, 11.171)
Log-rank p-value		0.268

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (94.2, 100.0)	94.8 (91.4, 98.1)
6 months	97.5 (94.2, 100.0)	93.7 (89.9, 97.6)
9 months	NE (NE, NE)	90.6 (83.5, 97.7)
12 months	NE (NE, NE)	90.6 (83.5, 97.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	2 (2.3)	8 (4.5)
Number of Subjects Censored, n (%)	86 (97.7)	171 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.736 (0.802)
95% CI		(0.361, 8.360)
Log-rank p-value		0.514

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (94.2, 100.0)	95.5 (92.5, 98.5)
6 months	97.5 (94.2, 100.0)	95.5 (92.5, 98.5)
9 months	NE (NE, NE)	95.5 (92.5, 98.5)
12 months	NE (NE, NE)	95.5 (92.5, 98.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	2 (2.3)	5 (2.8)
Number of Subjects Censored, n (%)	86 (97.7)	174 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.927 (0.853)
95% CI		(0.174, 4.937)
Log-rank p-value		0.936

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (93.7, 100.0)	96.9 (94.3, 99.6)
6 months	97.4 (93.7, 100.0)	96.9 (94.3, 99.6)
9 months	NE (NE, NE)	96.9 (94.3, 99.6)
12 months	NE (NE, NE)	96.9 (94.3, 99.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	5 (5.7)	1 (0.6)
Number of Subjects Censored, n (%)	83 (94.3)	178 (99.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.097 (1.097)
95% CI		(0.011, 0.836)
Log-rank p-value		0.008

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.6 (88.2, 99.0)	99.4 (98.3, 100.0)
6 months	93.6 (88.2, 99.0)	99.4 (98.3, 100.0)
9 months	NE (NE, NE)	99.4 (98.3, 100.0)
12 months	NE (NE, NE)	99.4 (98.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	9 (5.0)
Number of Subjects Censored, n (%)	88 (100.0)	170 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.033

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.7 (91.3, 98.1)
6 months	100.0 (100.0, 100.0)	94.7 (91.3, 98.1)
9 months	NE (NE, NE)	94.7 (91.3, 98.1)
12 months	NE (NE, NE)	94.7 (91.3, 98.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	28 (31.8)	74 (41.3)
Number of Subjects Censored, n (%)	60 (68.2)	105 (58.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.02 (0.69, NE)	1.54 (0.95, 1.91)
Median (95% CI)	NE (NE, NE)	NE (4.73, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.157 (0.225)
95% CI		(0.745, 1.798)
Log-rank p-value		0.573

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	68.3 (58.4, 78.3)	62.5 (55.2, 69.7)
6 months	64.9 (53.5, 76.4)	55.8 (47.7, 63.8)
9 months	NE (NE, NE)	51.5 (41.9, 61.1)
12 months	NE (NE, NE)	51.5 (41.9, 61.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.58	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	21 (23.9)	51 (28.5)
Number of Subjects Censored, n (%)	67 (76.1)	128 (71.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.89, NE)	2.92 (1.61, 6.97)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.068 (0.263)
95% CI		(0.638, 1.787)
Log-rank p-value		0.857

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.5 (66.4, 84.6)	73.5 (66.8, 80.2)
6 months	75.5 (66.4, 84.6)	68.8 (61.3, 76.2)
9 months	NE (NE, NE)	66.7 (58.4, 75.0)
12 months	NE (NE, NE)	66.7 (58.4, 75.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	8 (4.5)
Number of Subjects Censored, n (%)	87 (98.9)	171 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.607 (1.077)
95% CI		(0.316, 21.506)
Log-rank p-value		0.305

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.6, 100.0)	95.6 (92.3, 98.8)
6 months	98.8 (96.6, 100.0)	95.6 (92.3, 98.8)
9 months	NE (NE, NE)	92.5 (85.8, 99.2)
12 months	NE (NE, NE)	92.5 (85.8, 99.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	3 (3.4)	5 (2.8)
Number of Subjects Censored, n (%)	85 (96.6)	174 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.640 (0.750)
95% CI		(0.147, 2.785)
Log-rank p-value		0.565

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (94.4, 100.0)	97.7 (95.5, 99.9)
6 months	93.7 (85.6, 100.0)	96.6 (93.5, 99.7)
9 months	NE (NE, NE)	96.6 (93.5, 99.7)
12 months	NE (NE, NE)	96.6 (93.5, 99.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	6 (3.4)
Number of Subjects Censored, n (%)	87 (98.9)	173 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.806 (1.085)
95% CI		(0.335, 23.523)
Log-rank p-value		0.335

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.7, 100.0)	96.5 (93.7, 99.3)
6 months	98.5 (95.7, 100.0)	96.5 (93.7, 99.3)
9 months	NE (NE, NE)	96.5 (93.7, 99.3)
12 months	NE (NE, NE)	96.5 (93.7, 99.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	2 (1.1)
Number of Subjects Censored, n (%)	87 (98.9)	177 (98.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.563 (1.306)
95% CI		(0.044, 7.282)
Log-rank p-value		0.612

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.5, 100.0)	98.7 (97.0, 100.0)
6 months	98.8 (96.5, 100.0)	98.7 (97.0, 100.0)
9 months	NE (NE, NE)	98.7 (97.0, 100.0)
12 months	NE (NE, NE)	98.7 (97.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	9 (5.0)
Number of Subjects Censored, n (%)	88 (100.0)	170 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.078

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.4 (93.6, 99.2)
6 months	100.0 (100.0, 100.0)	93.7 (89.1, 98.4)
9 months	NE (NE, NE)	91.1 (84.4, 97.9)
12 months	NE (NE, NE)	91.1 (84.4, 97.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	4 (2.2)
Number of Subjects Censored, n (%)	87 (98.9)	175 (97.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.866 (1.124)
95% CI		(0.206, 16.886)
Log-rank p-value		0.569

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.6, 100.0)	97.6 (95.3, 99.9)
6 months	98.8 (96.6, 100.0)	97.6 (95.3, 99.9)
9 months	NE (NE, NE)	97.6 (95.3, 99.9)
12 months	NE (NE, NE)	97.6 (95.3, 99.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	5 (2.8)
Number of Subjects Censored, n (%)	87 (98.9)	174 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9*, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.072 (1.106)
95% CI		(0.237, 18.122)
Log-rank p-value		0.531

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.6, 100.0)	97.7 (95.4, 99.9)
6 months	98.8 (96.6, 100.0)	96.1 (92.3, 99.9)
9 months	NE (NE, NE)	96.1 (92.3, 99.9)
12 months	NE (NE, NE)	96.1 (92.3, 99.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	3 (1.7)
Number of Subjects Censored, n (%)	87 (98.9)	176 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.782 (1.160)
95% CI		(0.183, 17.314)
Log-rank p-value		0.675

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.6, 100.0)	98.2 (96.2, 100.0)
6 months	98.8 (96.6, 100.0)	98.2 (96.2, 100.0)
9 months	NE (NE, NE)	98.2 (96.2, 100.0)
12 months	NE (NE, NE)	98.2 (96.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	3 (1.7)
Number of Subjects Censored, n (%)	88 (100.0)	176 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.482

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.5 (96.4, 100.0)
6 months	100.0 (100.0, 100.0)	97.4 (94.5, 100.0)
9 months	NE (NE, NE)	97.4 (94.5, 100.0)
12 months	NE (NE, NE)	97.4 (94.5, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	22 (25.0)	74 (41.3)
Number of Subjects Censored, n (%)	66 (75.0)	105 (58.7)
Time to first TEAE (months)		
25% percentile (95% CI)	3.55 (1.35, NE)	1.61 (0.95, 2.46)
Median (95% CI)	NE (3.71, NE)	6.90 (4.73, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.452 (0.247)
95% CI		(0.894, 2.356)
Log-rank p-value		0.111

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.5 (66.0, 84.9)	64.1 (56.9, 71.4)
6 months	64.7 (48.6, 80.7)	56.5 (48.2, 64.9)
9 months	NE (NE, NE)	47.3 (37.0, 57.7)
12 months	NE (NE, NE)	47.3 (37.0, 57.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.73	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	11 (12.5)	20 (11.2)
Number of Subjects Censored, n (%)	77 (87.5)	159 (88.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.73, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.741 (0.384)
95% CI		(0.349, 1.572)
Log-rank p-value		0.412

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.1 (76.8, 93.4)	90.7 (86.3, 95.0)
6 months	85.1 (76.8, 93.4)	86.9 (81.0, 92.9)
9 months	NE (NE, NE)	85.3 (78.7, 91.9)
12 months	NE (NE, NE)	85.3 (78.7, 91.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	2 (2.3)	17 (9.5)
Number of Subjects Censored, n (%)	86 (97.7)	162 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.012 (0.755)
95% CI		(0.686, 13.227)
Log-rank p-value		0.119

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (94.5, 100.0)	92.0 (87.7, 96.2)
6 months	97.7 (94.5, 100.0)	89.0 (83.7, 94.3)
9 months	NE (NE, NE)	87.3 (81.2, 93.4)
12 months	NE (NE, NE)	87.3 (81.2, 93.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	20 (11.2)
Number of Subjects Censored, n (%)	87 (98.9)	159 (88.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.819 (1.030)
95% CI		(0.905, 51.356)
Log-rank p-value		0.030

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.6, 100.0)	91.5 (87.3, 95.8)
6 months	98.8 (96.6, 100.0)	87.6 (82.0, 93.2)
9 months	NE (NE, NE)	84.3 (77.2, 91.3)
12 months	NE (NE, NE)	84.3 (77.2, 91.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	3 (3.4)	11 (6.1)
Number of Subjects Censored, n (%)	85 (96.6)	168 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.4, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.312 (0.670)
95% CI		(0.353, 4.876)
Log-rank p-value		0.669

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.5 (92.6, 100.0)	95.3 (92.1, 98.5)
6 months	96.5 (92.6, 100.0)	93.3 (89.1, 97.5)
9 months	NE (NE, NE)	90.6 (84.0, 97.2)
12 months	NE (NE, NE)	90.6 (84.0, 97.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	14 (7.8)
Number of Subjects Censored, n (%)	88 (100.0)	165 (92.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (8.51, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.8, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.035

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.1 (90.5, 97.6)
6 months	100.0 (100.0, 100.0)	92.4 (87.5, 97.2)
9 months	NE (NE, NE)	84.2 (73.3, 95.1)
12 months	NE (NE, NE)	84.2 (73.3, 95.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	3 (3.4)	10 (5.6)
Number of Subjects Censored, n (%)	85 (96.6)	169 (94.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.186 (0.674)
95% CI		(0.317, 4.445)
Log-rank p-value		0.814

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.2 (92.0, 100.0)	95.1 (91.8, 98.5)
6 months	96.2 (92.0, 100.0)	94.1 (90.2, 98.0)
9 months	NE (NE, NE)	92.4 (87.4, 97.4)
12 months	NE (NE, NE)	92.4 (87.4, 97.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	5 (2.8)
Number of Subjects Censored, n (%)	88 (100.0)	174 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.156

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.7 (93.9, 99.6)
6 months	100.0 (100.0, 100.0)	96.7 (93.9, 99.6)
9 months	NE (NE, NE)	96.7 (93.9, 99.6)
12 months	NE (NE, NE)	96.7 (93.9, 99.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	3 (3.4)	7 (3.9)
Number of Subjects Censored, n (%)	85 (96.6)	172 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.55, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.787 (0.716)
95% CI		(0.193, 3.204)
Log-rank p-value		0.692

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (93.0, 100.0)	97.2 (94.7, 99.6)
6 months	92.0 (81.5, 100.0)	94.5 (90.1, 98.9)
9 months	NE (NE, NE)	94.5 (90.1, 98.9)
12 months	NE (NE, NE)	94.5 (90.1, 98.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	6 (3.4)
Number of Subjects Censored, n (%)	88 (100.0)	173 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.121

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.0 (94.4, 99.6)
6 months	100.0 (100.0, 100.0)	97.0 (94.4, 99.6)
9 months	NE (NE, NE)	94.7 (89.5, 99.8)
12 months	NE (NE, NE)	94.7 (89.5, 99.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	7 (3.9)
Number of Subjects Censored, n (%)	88 (100.0)	172 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.096

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.3 (93.3, 99.2)
6 months	100.0 (100.0, 100.0)	96.3 (93.3, 99.2)
9 months	NE (NE, NE)	93.9 (88.6, 99.3)
12 months	NE (NE, NE)	93.9 (88.6, 99.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	21 (23.9)	71 (39.7)
Number of Subjects Censored, n (%)	67 (76.1)	108 (60.3)
Time to first TEAE (months)		
25% percentile (95% CI)	2.40 (1.45, NE)	0.69 (0.59, 1.61)
Median (95% CI)	NE (NE, NE)	9.69 (6.41, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.713 (0.253)
95% CI		(1.044, 2.811)
Log-rank p-value		0.042

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	74.6 (65.1, 84.1)	62.8 (55.6, 70.0)
6 months	74.6 (65.1, 84.1)	59.2 (51.3, 67.1)
9 months	NE (NE, NE)	55.2 (46.0, 64.4)
12 months	NE (NE, NE)	49.7 (36.5, 62.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	2.53

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	6 (6.8)	34 (19.0)
Number of Subjects Censored, n (%)	82 (93.2)	145 (81.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.00, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.978 (0.448)
95% CI		(1.239, 7.161)
Log-rank p-value		0.013

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.9 (87.4, 98.4)	80.7 (74.9, 86.6)
6 months	92.9 (87.4, 98.4)	80.7 (74.9, 86.6)
9 months	NE (NE, NE)	80.7 (74.9, 86.6)
12 months	NE (NE, NE)	80.7 (74.9, 86.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	9 (10.2)	15 (8.4)
Number of Subjects Censored, n (%)	79 (89.8)	164 (91.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (10.28, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.2, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.570 (0.443)
95% CI		(0.239, 1.357)
Log-rank p-value		0.206

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.0 (82.2, 95.8)	93.2 (89.2, 97.1)
6 months	89.0 (82.2, 95.8)	91.2 (86.5, 95.9)
9 months	NE (NE, NE)	89.6 (84.0, 95.2)
12 months	NE (NE, NE)	81.5 (65.4, 97.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	7 (8.0)	17 (9.5)
Number of Subjects Censored, n (%)	81 (92.0)	162 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.080 (0.455)
95% CI		(0.443, 2.635)
Log-rank p-value		0.809

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.4 (85.2, 97.6)	89.9 (85.4, 94.5)
6 months	91.4 (85.2, 97.6)	89.9 (85.4, 94.5)
9 months	NE (NE, NE)	89.9 (85.4, 94.5)
12 months	NE (NE, NE)	89.9 (85.4, 94.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	7 (3.9)
Number of Subjects Censored, n (%)	87 (98.9)	172 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.549 (1.070)
95% CI		(0.436, 28.896)
Log-rank p-value		0.221

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.6, 100.0)	95.8 (92.8, 98.9)
6 months	98.8 (96.6, 100.0)	95.8 (92.8, 98.9)
9 months	NE (NE, NE)	95.8 (92.8, 98.9)
12 months	NE (NE, NE)	95.8 (92.8, 98.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	2 (1.1)
Number of Subjects Censored, n (%)	87 (98.9)	177 (98.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.5, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.849 (1.233)
95% CI		(0.076, 9.512)
Log-rank p-value		0.910

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.1, 100.0)	98.9 (97.3, 100.0)
6 months	98.7 (96.1, 100.0)	98.9 (97.3, 100.0)
9 months	NE (NE, NE)	98.9 (97.3, 100.0)
12 months	NE (NE, NE)	98.9 (97.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Vascular disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	14 (15.9)	70 (39.1)
Number of Subjects Censored, n (%)	74 (84.1)	109 (60.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.53, NE)	0.95 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	NE (6.93, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.653 (0.296)
95% CI		(1.486, 4.736)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Vascular disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.5 (75.2, 91.9)	63.0 (55.8, 70.2)
6 months	77.1 (62.8, 91.4)	59.1 (51.1, 67.1)
9 months	NE (NE, NE)	52.7 (41.7, 63.7)
12 months	NE (NE, NE)	52.7 (41.7, 63.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.74	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	9 (10.2)	68 (38.0)
Number of Subjects Censored, n (%)	79 (89.8)	111 (62.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.95 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	NE (6.93, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.097 (0.357)
95% CI		(2.036, 8.247)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.5 (81.3, 95.7)	63.5 (56.3, 70.6)
6 months	88.5 (81.3, 95.7)	60.8 (53.0, 68.6)
9 months	NE (NE, NE)	54.3 (43.2, 65.3)
12 months	NE (NE, NE)	54.3 (43.2, 65.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	27 (30.7)	65 (36.3)
Number of Subjects Censored, n (%)	61 (69.3)	114 (63.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.72, 3.71)	1.22 (0.72, 2.50)
Median (95% CI)	NE (3.71, NE)	NE (7.66, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.116 (0.232)
95% CI		(0.708, 1.760)
Log-rank p-value		0.556

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	69.0 (58.6, 79.4)	65.2 (58.1, 72.4)
6 months	57.5 (40.6, 74.4)	60.1 (51.8, 68.4)
9 months	NE (NE, NE)	56.6 (46.3, 66.9)
12 months	NE (NE, NE)	56.6 (46.3, 66.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	9 (10.2)	18 (10.1)
Number of Subjects Censored, n (%)	79 (89.8)	161 (89.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.924 (0.411)
95% CI		(0.412, 2.069)
Log-rank p-value		0.990

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.4 (82.9, 96.0)	89.7 (85.1, 94.4)
6 months	89.4 (82.9, 96.0)	88.8 (83.8, 93.7)
9 months	NE (NE, NE)	88.8 (83.8, 93.7)
12 months	NE (NE, NE)	88.8 (83.8, 93.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	5 (5.7)	26 (14.5)
Number of Subjects Censored, n (%)	83 (94.3)	153 (85.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.98, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.1, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.370 (0.493)
95% CI		(0.902, 6.226)
Log-rank p-value		0.078

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.1 (89.0, 99.1)	87.8 (82.9, 92.7)
6 months	94.1 (89.0, 99.1)	82.2 (75.0, 89.5)
9 months	NE (NE, NE)	78.5 (68.5, 88.4)
12 months	NE (NE, NE)	78.5 (68.5, 88.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	4 (4.5)	7 (3.9)
Number of Subjects Censored, n (%)	84 (95.5)	172 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.567 (0.658)
95% CI		(0.156, 2.057)
Log-rank p-value		0.379

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (94.6, 100.0)	96.5 (93.8, 99.3)
6 months	87.4 (73.6, 100.0)	95.1 (91.3, 99.0)
9 months	NE (NE, NE)	95.1 (91.3, 99.0)
12 months	NE (NE, NE)	95.1 (91.3, 99.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	2 (2.3)	6 (3.4)
Number of Subjects Censored, n (%)	86 (97.7)	173 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.419 (0.819)
95% CI		(0.285, 7.069)
Log-rank p-value		0.682

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (94.5, 100.0)	96.4 (93.5, 99.2)
6 months	97.7 (94.5, 100.0)	96.4 (93.5, 99.2)
9 months	NE (NE, NE)	96.4 (93.5, 99.2)
12 months	NE (NE, NE)	96.4 (93.5, 99.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	2 (1.1)
Number of Subjects Censored, n (%)	87 (98.9)	177 (98.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.8, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.939 (1.225)
95% CI		(0.085, 10.356)
Log-rank p-value		0.959

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.6, 100.0)	98.8 (97.2, 100.0)
6 months	98.8 (96.6, 100.0)	98.8 (97.2, 100.0)
9 months	NE (NE, NE)	98.8 (97.2, 100.0)
12 months	NE (NE, NE)	98.8 (97.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	3 (1.7)
Number of Subjects Censored, n (%)	88 (100.0)	176 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.8, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.304

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.1 (95.9, 100.0)
6 months	100.0 (100.0, 100.0)	98.1 (95.9, 100.0)
9 months	NE (NE, NE)	98.1 (95.9, 100.0)
12 months	NE (NE, NE)	98.1 (95.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	10 (11.4)	62 (34.6)
Number of Subjects Censored, n (%)	78 (88.6)	117 (65.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.45 (0.72, 2.07)
Median (95% CI)	NE (NE, NE)	13.14 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	13.14 (NE, NE)
Min, Max	0.1, 6.8*	0.0, 13.1
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.253 (0.344)
95% CI		(1.659, 6.379)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.2 (81.3, 95.1)	67.3 (60.3, 74.3)
6 months	88.2 (81.3, 95.1)	62.1 (53.9, 70.3)
9 months	NE (NE, NE)	62.1 (53.9, 70.3)
12 months	NE (NE, NE)	62.1 (53.9, 70.3)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.81	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	3 (3.4)	33 (18.4)
Number of Subjects Censored, n (%)	85 (96.6)	146 (81.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.58, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.799 (0.606)
95% CI		(1.769, 19.016)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.4 (92.4, 100.0)	82.6 (76.9, 88.3)
6 months	96.4 (92.4, 100.0)	79.0 (72.2, 85.8)
9 months	NE (NE, NE)	79.0 (72.2, 85.8)
12 months	NE (NE, NE)	79.0 (72.2, 85.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	4 (4.5)	7 (3.9)
Number of Subjects Censored, n (%)	84 (95.5)	172 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.827 (0.629)
95% CI		(0.241, 2.840)
Log-rank p-value		0.789

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (90.9, 99.8)	96.0 (93.1, 98.9)
6 months	95.4 (90.9, 99.8)	96.0 (93.1, 98.9)
9 months	NE (NE, NE)	96.0 (93.1, 98.9)
12 months	NE (NE, NE)	96.0 (93.1, 98.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	6 (3.4)
Number of Subjects Censored, n (%)	88 (100.0)	173 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.130

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.1 (94.5, 99.6)
6 months	100.0 (100.0, 100.0)	96.1 (92.9, 99.2)
9 months	NE (NE, NE)	96.1 (92.9, 99.2)
12 months	NE (NE, NE)	96.1 (92.9, 99.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Nervous system disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	11 (12.5)	45 (25.1)
Number of Subjects Censored, n (%)	77 (87.5)	134 (74.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.32 (1.61, NE)
Median (95% CI)	NE (NE, NE)	NE (11.10, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.773 (0.343)
95% CI		(0.905, 3.473)
Log-rank p-value		0.089

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Nervous system disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.5 (78.9, 94.0)	77.4 (71.1, 83.7)
6 months	86.5 (78.9, 94.0)	72.0 (64.1, 79.9)
9 months	NE (NE, NE)	70.2 (61.7, 78.6)
12 months	NE (NE, NE)	62.4 (46.1, 78.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	4 (4.5)	14 (7.8)
Number of Subjects Censored, n (%)	84 (95.5)	165 (92.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.569 (0.579)
95% CI		(0.504, 4.883)
Log-rank p-value		0.398

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.3 (90.8, 99.8)	92.7 (88.8, 96.5)
6 months	95.3 (90.8, 99.8)	92.7 (88.8, 96.5)
9 months	NE (NE, NE)	90.9 (85.8, 96.0)
12 months	NE (NE, NE)	90.9 (85.8, 96.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	5 (2.8)
Number of Subjects Censored, n (%)	87 (98.9)	174 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.4, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.947 (1.108)
95% CI		(0.222, 17.072)
Log-rank p-value		0.540

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.5, 100.0)	97.1 (94.6, 99.6)
6 months	98.8 (96.5, 100.0)	97.1 (94.6, 99.6)
9 months	NE (NE, NE)	97.1 (94.6, 99.6)
12 months	NE (NE, NE)	97.1 (94.6, 99.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	2 (1.1)
Number of Subjects Censored, n (%)	87 (98.9)	177 (98.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.6, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.131 (1.229)
95% CI		(0.102, 12.588)
Log-rank p-value		0.964

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.4, 100.0)	98.9 (97.3, 100.0)
6 months	98.8 (96.4, 100.0)	98.9 (97.3, 100.0)
9 months	NE (NE, NE)	98.9 (97.3, 100.0)
12 months	NE (NE, NE)	98.9 (97.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.24

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	12 (13.6)	44 (24.6)
Number of Subjects Censored, n (%)	76 (86.4)	135 (75.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.06 (3.35, NE)
Median (95% CI)	NE (NE, NE)	13.60 (11.96, NE)
75% percentile (95% CI)	NE (NE, NE)	13.60 (NE, NE)
Min, Max	0.0, 6.8*	0.0, 13.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.380 (0.333)
95% CI		(0.719, 2.651)
Log-rank p-value		0.417

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.4 (77.8, 93.1)	82.0 (76.3, 87.8)
6 months	85.4 (77.8, 93.1)	70.6 (62.1, 79.0)
9 months	NE (NE, NE)	68.1 (58.7, 77.5)
12 months	NE (NE, NE)	54.5 (29.5, 79.6)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.78	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	6 (6.8)	27 (15.1)
Number of Subjects Censored, n (%)	82 (93.2)	152 (84.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	8.38 (5.78, NE)
Median (95% CI)	NE (NE, NE)	13.60 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	13.60 (NE, NE)
Min, Max	0.2*, 6.8*	0.5, 13.6
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.481 (0.465)
95% CI		(0.596, 3.682)
Log-rank p-value		0.411

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.6 (86.9, 98.3)	90.5 (86.1, 95.0)
6 months	92.6 (86.9, 98.3)	81.5 (74.2, 88.9)
9 months	NE (NE, NE)	75.0 (63.6, 86.3)
12 months	NE (NE, NE)	75.0 (63.6, 86.3)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	2 (2.3)	6 (3.4)
Number of Subjects Censored, n (%)	86 (97.7)	173 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.308 (0.823)
95% CI		(0.261, 6.562)
Log-rank p-value		0.797

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (94.6, 100.0)	97.1 (94.7, 99.6)
6 months	97.7 (94.6, 100.0)	96.1 (92.9, 99.3)
9 months	NE (NE, NE)	96.1 (92.9, 99.3)
12 months	NE (NE, NE)	96.1 (92.9, 99.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Infections and infestations**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	12 (13.6)	44 (24.6)
Number of Subjects Censored, n (%)	76 (86.4)	135 (75.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.15, NE)	5.09 (2.96, 6.93)
Median (95% CI)	NE (NE, NE)	NE (7.69, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.214 (0.338)
95% CI		(0.626, 2.355)
Log-rank p-value		0.497

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Infections and infestations**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (80.2, 94.8)	81.8 (75.8, 87.8)
6 months	78.3 (64.2, 92.3)	70.9 (62.2, 79.6)
9 months	NE (NE, NE)	57.5 (44.4, 70.6)
12 months	NE (NE, NE)	57.5 (44.4, 70.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	3 (3.4)	8 (4.5)
Number of Subjects Censored, n (%)	85 (96.6)	171 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.4, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.862 (0.711)
95% CI		(0.214, 3.470)
Log-rank p-value		0.866

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.4 (93.6, 99.2)
6 months	81.9 (61.7, 100.0)	96.4 (93.6, 99.2)
9 months	NE (NE, NE)	92.2 (85.8, 98.6)
12 months	NE (NE, NE)	92.2 (85.8, 98.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	4 (4.5)	4 (2.2)
Number of Subjects Censored, n (%)	84 (95.5)	175 (97.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.295 (0.740)
95% CI		(0.069, 1.258)
Log-rank p-value		0.059

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.0 (90.1, 99.8)	98.8 (97.1, 100.0)
6 months	95.0 (90.1, 99.8)	96.1 (92.1, 100.0)
9 months	NE (NE, NE)	96.1 (92.1, 100.0)
12 months	NE (NE, NE)	96.1 (92.1, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.21

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	3 (1.7)
Number of Subjects Censored, n (%)	88 (100.0)	176 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.247

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.1 (95.9, 100.0)
6 months	100.0 (100.0, 100.0)	98.1 (95.9, 100.0)
9 months	NE (NE, NE)	98.1 (95.9, 100.0)
12 months	NE (NE, NE)	98.1 (95.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	17 (19.3)	30 (16.8)
Number of Subjects Censored, n (%)	71 (80.7)	149 (83.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.84, NE)	NE (5.85, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.625 (0.316)
95% CI		(0.337, 1.162)
Log-rank p-value		0.162

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.2 (68.8, 87.6)	87.3 (82.4, 92.3)
6 months	78.2 (68.8, 87.6)	81.7 (74.9, 88.5)
9 months	NE (NE, NE)	75.9 (67.0, 84.9)
12 months	NE (NE, NE)	75.9 (67.0, 84.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	15 (17.0)	14 (7.8)
Number of Subjects Censored, n (%)	73 (83.0)	165 (92.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.33, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.284 (0.394)
95% CI		(0.131, 0.614)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.2 (71.1, 89.4)	95.8 (92.7, 98.9)
6 months	80.2 (71.1, 89.4)	89.8 (83.7, 95.8)
9 months	NE (NE, NE)	86.3 (78.8, 93.8)
12 months	NE (NE, NE)	86.3 (78.8, 93.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	2 (2.3)	13 (7.3)
Number of Subjects Censored, n (%)	86 (97.7)	166 (92.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.787 (0.765)
95% CI		(0.622, 12.478)
Log-rank p-value		0.158

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.6 (94.3, 100.0)	92.7 (88.8, 96.5)
6 months	97.6 (94.3, 100.0)	92.7 (88.8, 96.5)
9 months	NE (NE, NE)	92.7 (88.8, 96.5)
12 months	NE (NE, NE)	92.7 (88.8, 96.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Endocrine disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	41 (22.9)
Number of Subjects Censored, n (%)	88 (100.0)	138 (77.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.98 (2.10, NE)
Median (95% CI)	NE (NE, NE)	NE (9.33, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Endocrine disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	78.5 (72.2, 84.8)
6 months	100.0 (100.0, 100.0)	74.1 (66.3, 81.8)
9 months	NE (NE, NE)	72.1 (63.6, 80.6)
12 months	NE (NE, NE)	64.1 (47.5, 80.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	36 (20.1)
Number of Subjects Censored, n (%)	88 (100.0)	143 (79.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	9.33 (2.79, NE)
Median (95% CI)	NE (NE, NE)	NE (9.33, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	81.5 (75.5, 87.4)
6 months	100.0 (100.0, 100.0)	77.1 (69.6, 84.6)
9 months	NE (NE, NE)	75.1 (66.8, 83.3)
12 months	NE (NE, NE)	67.6 (51.8, 83.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	7 (8.0)	27 (15.1)
Number of Subjects Censored, n (%)	81 (92.0)	152 (84.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.90, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.388 (0.433)
95% CI		(0.594, 3.242)
Log-rank p-value		0.345

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (86.4, 98.3)	86.8 (81.4, 92.1)
6 months	88.6 (79.5, 97.7)	81.5 (74.7, 88.3)
9 months	NE (NE, NE)	79.4 (71.7, 87.1)
12 months	NE (NE, NE)	79.4 (71.7, 87.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.52

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	4 (4.5)	15 (8.4)
Number of Subjects Censored, n (%)	84 (95.5)	164 (91.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.246 (0.575)
95% CI		(0.404, 3.844)
Log-rank p-value		0.512

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (90.1, 99.8)	92.9 (88.7, 97.0)
6 months	94.9 (90.1, 99.8)	89.9 (84.8, 95.1)
9 months	NE (NE, NE)	87.9 (81.6, 94.3)
12 months	NE (NE, NE)	87.9 (81.6, 94.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	2 (2.3)	6 (3.4)
Number of Subjects Censored, n (%)	86 (97.7)	173 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.099 (0.824)
95% CI		(0.219, 5.523)
Log-rank p-value		0.953

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.3, 100.0)	96.6 (93.6, 99.6)
6 months	94.9 (87.3, 100.0)	95.2 (91.2, 99.2)
9 months	NE (NE, NE)	95.2 (91.2, 99.2)
12 months	NE (NE, NE)	95.2 (91.2, 99.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	2 (2.3)	0
Number of Subjects Censored, n (%)	86 (97.7)	179 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.072

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (93.8, 100.0)	100.0 (100.0, 100.0)
6 months	97.4 (93.8, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.50

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	13 (14.8)	24 (13.4)
Number of Subjects Censored, n (%)	75 (85.2)	155 (86.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.15, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.728 (0.350)
95% CI		(0.367, 1.445)
Log-rank p-value		0.340

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.8 (78.4, 93.3)	86.8 (81.7, 92.0)
6 months	82.4 (72.7, 92.1)	84.4 (78.3, 90.4)
9 months	NE (NE, NE)	84.4 (78.3, 90.4)
12 months	NE (NE, NE)	84.4 (78.3, 90.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	2 (2.3)	8 (4.5)
Number of Subjects Censored, n (%)	86 (97.7)	171 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.9*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.364 (0.806)
95% CI		(0.281, 6.618)
Log-rank p-value		0.726

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.4 (93.9, 100.0)	95.5 (92.3, 98.8)
6 months	97.4 (93.9, 100.0)	93.9 (89.5, 98.4)
9 months	NE (NE, NE)	93.9 (89.5, 98.4)
12 months	NE (NE, NE)	93.9 (89.5, 98.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	6 (3.4)
Number of Subjects Censored, n (%)	87 (98.9)	173 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.978 (1.080)
95% CI		(0.358, 24.743)
Log-rank p-value		0.288

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Yes

Statistics	Placebo + BSC N=88	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.6, 100.0)	96.6 (93.9, 99.3)
6 months	98.8 (96.6, 100.0)	96.6 (93.9, 99.3)
9 months	NE (NE, NE)	96.6 (93.9, 99.3)
12 months	NE (NE, NE)	96.6 (93.9, 99.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	75 (52.8)	185 (66.8)
Number of Subjects Censored, n (%)	67 (47.2)	92 (33.2)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.49, 0.72)	0.59 (0.36, 0.69)
Median (95% CI)	1.87 (1.38, NE)	1.31 (0.95, 1.61)
75% percentile (95% CI)	NE (NE, NE)	NE (4.50, NE)
Min, Max	0.0, 13.0*	0.0, 12.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.348 (0.138)
95% CI		(1.028, 1.767)
Log-rank p-value		0.035

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	45.9 (37.4, 54.5)	38.1 (32.3, 43.9)
6 months	43.4 (34.0, 52.8)	27.2 (20.9, 33.5)
9 months	43.4 (34.0, 52.8)	27.2 (20.9, 33.5)
12 months	43.4 (34.0, 52.8)	27.2 (20.9, 33.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.64	1.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	29 (20.4)	88 (31.8)
Number of Subjects Censored, n (%)	113 (79.6)	189 (68.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.61, NE)	1.41 (0.85, 3.12)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.499 (0.216)
95% CI		(0.982, 2.287)
Log-rank p-value		0.054

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.0 (72.0, 86.0)	70.4 (64.9, 75.9)
6 months	75.9 (66.8, 84.9)	65.9 (59.8, 72.0)
9 months	75.9 (66.8, 84.9)	62.6 (54.0, 71.1)
12 months	75.9 (66.8, 84.9)	62.6 (54.0, 71.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.37	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	22 (15.5)	54 (19.5)
Number of Subjects Censored, n (%)	120 (84.5)	223 (80.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.71, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.191 (0.255)
95% CI		(0.722, 1.963)
Log-rank p-value		0.396

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.4 (76.9, 89.8)	80.9 (76.2, 85.7)
6 months	83.4 (76.9, 89.8)	78.6 (73.2, 83.9)
9 months	83.4 (76.9, 89.8)	78.6 (73.2, 83.9)
12 months	83.4 (76.9, 89.8)	78.6 (73.2, 83.9)
18 months	NE (NE, NE)	78.6 (73.2, 83.9)
Median Follow-up Time (months)	2.37	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	12 (8.5)	20 (7.2)
Number of Subjects Censored, n (%)	130 (91.5)	257 (92.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.734 (0.373)
95% CI		(0.353, 1.525)
Log-rank p-value		0.377

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.4 (85.1, 95.8)	93.7 (90.7, 96.6)
6 months	90.4 (85.1, 95.8)	92.6 (89.1, 96.2)
9 months	90.4 (85.1, 95.8)	91.4 (87.1, 95.6)
12 months	90.4 (85.1, 95.8)	83.1 (67.1, 99.1)
18 months	NE (NE, NE)	83.1 (67.1, 99.1)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	5 (3.5)	39 (14.1)
Number of Subjects Censored, n (%)	137 (96.5)	238 (85.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
Median (95% CI)	NE (NE, NE)	13.24 (13.24, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.24, NE)
Min, Max	0.4*, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.939 (0.477)
95% CI		(1.546, 10.038)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.1 (92.7, 99.5)	87.1 (83.1, 91.1)
6 months	96.1 (92.7, 99.5)	85.6 (81.2, 90.1)
9 months	96.1 (92.7, 99.5)	84.0 (78.6, 89.4)
12 months	96.1 (92.7, 99.5)	84.0 (78.6, 89.4)
18 months	NE (NE, NE)	42.0 (0.0, 100.0)
Median Follow-up Time (months)	2.79	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	17 (12.0)	16 (5.8)
Number of Subjects Censored, n (%)	125 (88.0)	261 (94.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.358 (0.359)
95% CI		(0.177, 0.724)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.8 (80.9, 92.7)	96.2 (93.9, 98.5)
6 months	86.8 (80.9, 92.7)	92.4 (88.3, 96.5)
9 months	86.8 (80.9, 92.7)	92.4 (88.3, 96.5)
12 months	86.8 (80.9, 92.7)	92.4 (88.3, 96.5)
18 months	NE (NE, NE)	80.9 (59.4, 100.0)
Median Follow-up Time (months)	2.81	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	12 (8.5)	15 (5.4)
Number of Subjects Censored, n (%)	130 (91.5)	262 (94.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.562 (0.393)
95% CI		(0.260, 1.215)
Log-rank p-value		0.139

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.8 (85.7, 95.9)	94.7 (92.0, 97.4)
6 months	90.8 (85.7, 95.9)	94.7 (92.0, 97.4)
9 months	90.8 (85.7, 95.9)	94.7 (92.0, 97.4)
12 months	90.8 (85.7, 95.9)	90.4 (81.8, 99.1)
18 months	NE (NE, NE)	90.4 (81.8, 99.1)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	4 (2.8)	5 (1.8)
Number of Subjects Censored, n (%)	138 (97.2)	272 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.494 (0.696)
95% CI		(0.126, 1.931)
Log-rank p-value		0.340

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.9 (93.8, 99.9)	98.5 (97.0, 100.0)
6 months	96.9 (93.8, 99.9)	98.5 (97.0, 100.0)
9 months	96.9 (93.8, 99.9)	98.5 (97.0, 100.0)
12 months	96.9 (93.8, 99.9)	94.2 (85.9, 100.0)
18 months	NE (NE, NE)	94.2 (85.9, 100.0)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	3 (2.1)	5 (1.8)
Number of Subjects Censored, n (%)	139 (97.9)	272 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.580 (0.749)
95% CI		(0.134, 2.519)
Log-rank p-value		0.427

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (95.1, 100.0)	98.8 (97.5, 100.0)
6 months	97.7 (95.1, 100.0)	97.2 (94.7, 99.8)
9 months	97.7 (95.1, 100.0)	97.2 (94.7, 99.8)
12 months	97.7 (95.1, 100.0)	97.2 (94.7, 99.8)
18 months	NE (NE, NE)	97.2 (94.7, 99.8)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	2 (1.4)	7 (2.5)
Number of Subjects Censored, n (%)	140 (98.6)	270 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.430 (0.825)
95% CI		(0.284, 7.198)
Log-rank p-value		0.623

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.6, 100.0)	98.2 (96.6, 99.8)
6 months	98.6 (96.6, 100.0)	96.9 (94.0, 99.8)
9 months	98.6 (96.6, 100.0)	94.0 (87.7, 100.0)
12 months	98.6 (96.6, 100.0)	94.0 (87.7, 100.0)
18 months	NE (NE, NE)	94.0 (87.7, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	73 (51.4)	190 (68.6)
Number of Subjects Censored, n (%)	69 (48.6)	87 (31.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.46, 0.72)	0.56 (0.43, 0.69)
Median (95% CI)	2.00 (1.45, 5.59)	1.45 (0.92, 1.94)
75% percentile (95% CI)	5.59 (5.36, NE)	5.55 (4.70, 7.62)
Min, Max	0.0, 6.4*	0.0, 11.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.244 (0.140)
95% CI		(0.945, 1.636)
Log-rank p-value		0.091

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	47.2 (38.4, 56.0)	38.7 (32.8, 44.6)
6 months	21.2 (0.0, 42.9)	23.0 (16.3, 29.6)
9 months	NE (NE, NE)	16.4 (9.1, 23.7)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.56	1.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	15 (10.6)	65 (23.5)
Number of Subjects Censored, n (%)	127 (89.4)	212 (76.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.55 (2.89, NE)
Median (95% CI)	NE (NE, NE)	NE (10.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.945 (0.290)
95% CI		(1.102, 3.433)
Log-rank p-value		0.021

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.0 (83.7, 94.3)	79.8 (75.0, 84.7)
6 months	89.0 (83.7, 94.3)	73.5 (67.2, 79.8)
9 months	89.0 (83.7, 94.3)	70.1 (62.5, 77.7)
12 months	89.0 (83.7, 94.3)	62.3 (46.4, 78.2)
18 months	NE (NE, NE)	62.3 (46.4, 78.2)
Median Follow-up Time (months)	2.50	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	24 (16.9)	46 (16.6)
Number of Subjects Censored, n (%)	118 (83.1)	231 (83.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (5.29, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.726 (0.259)
95% CI		(0.437, 1.206)
Log-rank p-value		0.227

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.8 (76.2, 89.3)	85.7 (81.4, 90.0)
6 months	77.6 (66.0, 89.2)	78.6 (72.4, 84.9)
9 months	77.6 (66.0, 89.2)	76.4 (69.0, 83.8)
12 months	77.6 (66.0, 89.2)	76.4 (69.0, 83.8)
18 months	NE (NE, NE)	76.4 (69.0, 83.8)
Median Follow-up Time (months)	2.58	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	19 (13.4)	52 (18.8)
Number of Subjects Censored, n (%)	123 (86.6)	225 (81.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	12.25 (4.21, NE)
Median (95% CI)	NE (NE, NE)	NE (12.25, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.071 (0.274)
95% CI		(0.626, 1.834)
Log-rank p-value		0.599

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.5 (79.4, 91.6)	83.5 (78.8, 88.1)
6 months	85.5 (79.4, 91.6)	77.7 (71.7, 83.8)
9 months	85.5 (79.4, 91.6)	75.3 (68.5, 82.0)
12 months	85.5 (79.4, 91.6)	75.3 (68.5, 82.0)
18 months	NE (NE, NE)	62.7 (39.6, 85.9)
Median Follow-up Time (months)	2.61	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	8 (5.6)	44 (15.9)
Number of Subjects Censored, n (%)	134 (94.4)	233 (84.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	9.33 (6.70, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.119 (0.390)
95% CI		(0.987, 4.552)
Log-rank p-value		0.051

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.3 (90.4, 98.1)	86.5 (82.3, 90.8)
6 months	94.3 (90.4, 98.1)	82.4 (77.2, 87.6)
9 months	94.3 (90.4, 98.1)	77.1 (69.4, 84.7)
12 months	94.3 (90.4, 98.1)	73.8 (64.3, 83.4)
18 months	NE (NE, NE)	73.8 (64.3, 83.4)
Median Follow-up Time (months)	2.79	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	17 (12.0)	37 (13.4)
Number of Subjects Censored, n (%)	125 (88.0)	240 (86.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.36, NE)	18.04 (7.10, NE)
Median (95% CI)	NE (NE, NE)	NE (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.836 (0.302)
95% CI		(0.463, 1.510)
Log-rank p-value		0.706

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.9 (82.3, 93.5)	89.7 (86.0, 93.4)
6 months	79.1 (62.0, 96.2)	83.1 (77.4, 88.8)
9 months	79.1 (62.0, 96.2)	81.3 (74.7, 87.9)
12 months	79.1 (62.0, 96.2)	81.3 (74.7, 87.9)
18 months	NE (NE, NE)	81.3 (74.7, 87.9)
Median Follow-up Time (months)	2.79	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	1 (0.7)	38 (13.7)
Number of Subjects Censored, n (%)	141 (99.3)	239 (86.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		18.721 (1.015)
95% CI		(2.562, 136.829)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	87.3 (83.4, 91.3)
6 months	99.3 (97.8, 100.0)	85.0 (80.4, 89.7)
9 months	99.3 (97.8, 100.0)	83.4 (77.8, 89.0)
12 months	99.3 (97.8, 100.0)	83.4 (77.8, 89.0)
18 months	NE (NE, NE)	83.4 (77.8, 89.0)
Median Follow-up Time (months)	2.81	3.48

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	6 (4.2)	23 (8.3)
Number of Subjects Censored, n (%)	136 (95.8)	254 (91.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.614 (0.465)
95% CI		(0.648, 4.017)
Log-rank p-value		0.318

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.4 (93.2, 99.5)	93.2 (90.2, 96.2)
6 months	84.3 (62.1, 100.0)	89.2 (84.7, 93.8)
9 months	NE (NE, NE)	89.2 (84.7, 93.8)
12 months	NE (NE, NE)	89.2 (84.7, 93.8)
18 months	NE (NE, NE)	89.2 (84.7, 93.8)
Median Follow-up Time (months)	2.79	3.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	2 (1.4)	8 (2.9)
Number of Subjects Censored, n (%)	140 (98.6)	269 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.155 (0.834)
95% CI		(0.225, 5.924)
Log-rank p-value		0.816

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.6, 100.0)	98.2 (96.6, 99.8)
6 months	98.6 (96.6, 100.0)	96.3 (93.2, 99.3)
9 months	98.6 (96.6, 100.0)	94.2 (89.1, 99.2)
12 months	98.6 (96.6, 100.0)	94.2 (89.1, 99.2)
18 months	NE (NE, NE)	94.2 (89.1, 99.2)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	2 (1.4)	6 (2.2)
Number of Subjects Censored, n (%)	140 (98.6)	271 (97.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.459 (0.817)
95% CI		(0.294, 7.242)
Log-rank p-value		0.655

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.3, 100.0)	97.8 (96.0, 99.5)
6 months	98.4 (96.3, 100.0)	97.8 (96.0, 99.5)
9 months	98.4 (96.3, 100.0)	97.8 (96.0, 99.5)
12 months	98.4 (96.3, 100.0)	97.8 (96.0, 99.5)
18 months	NE (NE, NE)	97.8 (96.0, 99.5)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	6 (4.2)	2 (0.7)
Number of Subjects Censored, n (%)	136 (95.8)	275 (99.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.114 (0.873)
95% CI		(0.021, 0.633)
Log-rank p-value		0.004

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (92.3, 99.1)	99.6 (98.8, 100.0)
6 months	95.7 (92.3, 99.1)	98.4 (95.9, 100.0)
9 months	95.7 (92.3, 99.1)	98.4 (95.9, 100.0)
12 months	95.7 (92.3, 99.1)	98.4 (95.9, 100.0)
18 months	NE (NE, NE)	98.4 (95.9, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	0	4 (1.4)
Number of Subjects Censored, n (%)	142 (100.0)	273 (98.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.237

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.8 (97.5, 100.0)
6 months	100.0 (100.0, 100.0)	98.8 (97.5, 100.0)
9 months	100.0 (100.0, 100.0)	96.5 (91.9, 100.0)
12 months	100.0 (100.0, 100.0)	96.5 (91.9, 100.0)
18 months	NE (NE, NE)	96.5 (91.9, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	35 (24.6)	122 (44.0)
Number of Subjects Censored, n (%)	107 (75.4)	155 (56.0)
Time to first TEAE (months)		
25% percentile (95% CI)	4.27 (0.95, NE)	1.18 (0.72, 1.64)
Median (95% CI)	10.18 (NE, NE)	6.24 (3.68, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.0, 10.2	0.0, 12.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.591 (0.194)
95% CI		(1.088, 2.327)
Log-rank p-value		0.016

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.3 (67.8, 82.7)	58.7 (52.6, 64.8)
6 months	69.5 (56.6, 82.4)	51.4 (44.4, 58.5)
9 months	69.5 (56.6, 82.4)	46.2 (38.2, 54.2)
12 months	0.0 (NE, NE)	42.0 (31.3, 52.7)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.43	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	19 (13.4)	73 (26.4)
Number of Subjects Censored, n (%)	123 (86.6)	204 (73.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.27, NE)	2.99 (1.84, 9.43)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.755 (0.260)
95% CI		(1.054, 2.923)
Log-rank p-value		0.033

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.1 (80.1, 92.1)	74.6 (69.3, 80.0)
6 months	80.7 (69.1, 92.4)	71.6 (65.7, 77.6)
9 months	80.7 (69.1, 92.4)	69.1 (62.3, 75.8)
12 months	80.7 (69.1, 92.4)	65.6 (56.4, 74.8)
18 months	NE (NE, NE)	65.6 (56.4, 74.8)
Median Follow-up Time (months)	2.58	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	3 (2.1)	20 (7.2)
Number of Subjects Censored, n (%)	139 (97.9)	257 (92.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.762 (0.623)
95% CI		(0.814, 9.375)
Log-rank p-value		0.088

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.9 (95.5, 100.0)	92.9 (89.8, 96.1)
6 months	97.9 (95.5, 100.0)	91.5 (87.8, 95.2)
9 months	97.9 (95.5, 100.0)	91.5 (87.8, 95.2)
12 months	97.9 (95.5, 100.0)	91.5 (87.8, 95.2)
18 months	NE (NE, NE)	91.5 (87.8, 95.2)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	2 (1.4)	15 (5.4)
Number of Subjects Censored, n (%)	140 (98.6)	262 (94.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.692 (0.762)
95% CI		(0.605, 11.981)
Log-rank p-value		0.179

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.6, 100.0)	95.7 (93.2, 98.2)
6 months	98.6 (96.6, 100.0)	93.0 (89.1, 96.9)
9 months	98.6 (96.6, 100.0)	91.2 (85.9, 96.4)
12 months	98.6 (96.6, 100.0)	91.2 (85.9, 96.4)
18 months	NE (NE, NE)	91.2 (85.9, 96.4)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	3 (2.1)	8 (2.9)
Number of Subjects Censored, n (%)	139 (97.9)	269 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.090 (0.693)
95% CI		(0.280, 4.238)
Log-rank p-value		0.834

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.9 (95.5, 100.0)	97.7 (95.8, 99.5)
6 months	97.9 (95.5, 100.0)	97.0 (94.8, 99.3)
9 months	97.9 (95.5, 100.0)	94.2 (88.2, 100.0)
12 months	97.9 (95.5, 100.0)	94.2 (88.2, 100.0)
18 months	NE (NE, NE)	94.2 (88.2, 100.0)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	2 (1.4)	13 (4.7)
Number of Subjects Censored, n (%)	140 (98.6)	264 (95.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.612 (0.771)
95% CI		(0.576, 11.844)
Log-rank p-value		0.192

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.6, 100.0)	95.8 (93.3, 98.2)
6 months	98.6 (96.6, 100.0)	94.7 (91.6, 97.9)
9 months	98.6 (96.6, 100.0)	92.8 (88.0, 97.6)
12 months	98.6 (96.6, 100.0)	92.8 (88.0, 97.6)
18 months	NE (NE, NE)	92.8 (88.0, 97.6)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	0	9 (3.2)
Number of Subjects Censored, n (%)	142 (100.0)	268 (96.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.065

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.0 (95.0, 99.1)
6 months	100.0 (100.0, 100.0)	96.2 (93.5, 98.8)
9 months	100.0 (100.0, 100.0)	96.2 (93.5, 98.8)
12 months	100.0 (100.0, 100.0)	96.2 (93.5, 98.8)
18 months	NE (NE, NE)	96.2 (93.5, 98.8)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	2 (1.4)	9 (3.2)
Number of Subjects Censored, n (%)	140 (98.6)	268 (96.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.797 (0.790)
95% CI		(0.382, 8.446)
Log-rank p-value		0.450

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (94.7, 100.0)	96.9 (94.7, 99.0)
6 months	97.8 (94.7, 100.0)	96.9 (94.7, 99.0)
9 months	97.8 (94.7, 100.0)	95.5 (92.1, 98.9)
12 months	97.8 (94.7, 100.0)	95.5 (92.1, 98.9)
18 months	NE (NE, NE)	95.5 (92.1, 98.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	1 (0.7)	8 (2.9)
Number of Subjects Censored, n (%)	141 (99.3)	269 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.801 (1.079)
95% CI		(0.338, 23.226)
Log-rank p-value		0.280

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	98.1 (96.4, 99.8)
6 months	99.3 (97.9, 100.0)	97.5 (95.4, 99.5)
9 months	99.3 (97.9, 100.0)	93.4 (87.3, 99.6)
12 months	99.3 (97.9, 100.0)	93.4 (87.3, 99.6)
18 months	NE (NE, NE)	93.4 (87.3, 99.6)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	2 (1.4)	8 (2.9)
Number of Subjects Censored, n (%)	140 (98.6)	269 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Median (95% CI)	10.18 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 10.2	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.611 (0.802)
95% CI		(0.334, 7.760)
Log-rank p-value		0.564

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	96.9 (94.9, 99.0)
6 months	99.3 (97.9, 100.0)	96.9 (94.9, 99.0)
9 months	99.3 (97.9, 100.0)	96.9 (94.9, 99.0)
12 months	0.0 (NE, NE)	96.9 (94.9, 99.0)
18 months	0.0 (NE, NE)	96.9 (94.9, 99.0)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	1 (0.7)	8 (2.9)
Number of Subjects Censored, n (%)	141 (99.3)	269 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.809 (1.099)
95% CI		(0.210, 15.581)
Log-rank p-value		0.539

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.6, 100.0)	98.9 (97.7, 100.0)
6 months	99.2 (97.6, 100.0)	94.3 (90.2, 98.5)
9 months	99.2 (97.6, 100.0)	94.3 (90.2, 98.5)
12 months	99.2 (97.6, 100.0)	94.3 (90.2, 98.5)
18 months	NE (NE, NE)	94.3 (90.2, 98.5)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	41 (28.9)	112 (40.4)
Number of Subjects Censored, n (%)	101 (71.1)	165 (59.6)
Time to first TEAE (months)		
25% percentile (95% CI)	1.61 (0.92, 5.82)	1.58 (0.95, 1.84)
Median (95% CI)	5.82 (5.59, NE)	7.85 (5.78, NE)
75% percentile (95% CI)	NE (5.82, NE)	NE (16.79, NE)
Min, Max	0.0, 6.5*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.184 (0.186)
95% CI		(0.822, 1.704)
Log-rank p-value		0.394

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.0 (63.3, 78.8)	62.4 (56.5, 68.3)
6 months	45.7 (15.9, 75.4)	55.2 (48.1, 62.3)
9 months	NE (NE, NE)	49.6 (41.2, 57.9)
12 months	NE (NE, NE)	49.6 (41.2, 57.9)
18 months	NE (NE, NE)	37.2 (15.2, 59.1)
Median Follow-up Time (months)	2.51	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	10 (7.0)	36 (13.0)
Number of Subjects Censored, n (%)	132 (93.0)	241 (87.0)
Time to first TEAE (months)		
25% percentile (95% CI)	5.82 (5.59, NE)	NE (7.85, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (5.82, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.443 (0.365)
95% CI		(0.706, 2.950)
Log-rank p-value		0.308

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.1 (88.3, 97.9)	88.3 (84.4, 92.3)
6 months	65.1 (31.7, 98.6)	84.8 (79.7, 90.0)
9 months	NE (NE, NE)	81.2 (74.1, 88.2)
12 months	NE (NE, NE)	81.2 (74.1, 88.2)
18 months	NE (NE, NE)	81.2 (74.1, 88.2)
Median Follow-up Time (months)	2.79	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	9 (6.3)	31 (11.2)
Number of Subjects Censored, n (%)	133 (93.7)	246 (88.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.452 (0.387)
95% CI		(0.681, 3.099)
Log-rank p-value		0.396

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.2 (90.2, 98.1)	90.1 (86.4, 93.7)
6 months	82.4 (60.5, 100.0)	87.2 (82.3, 92.0)
9 months	NE (NE, NE)	83.8 (77.3, 90.3)
12 months	NE (NE, NE)	83.8 (77.3, 90.3)
18 months	NE (NE, NE)	83.8 (77.3, 90.3)
Median Follow-up Time (months)	2.81	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	8 (5.6)	27 (9.7)
Number of Subjects Censored, n (%)	134 (94.4)	250 (90.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.437 (0.410)
95% CI		(0.643, 3.211)
Log-rank p-value		0.424

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.0 (91.3, 98.6)	91.3 (87.9, 94.7)
6 months	83.1 (61.1, 100.0)	89.3 (85.0, 93.6)
9 months	NE (NE, NE)	85.9 (79.7, 92.1)
12 months	NE (NE, NE)	85.9 (79.7, 92.1)
18 months	NE (NE, NE)	85.9 (79.7, 92.1)
Median Follow-up Time (months)	2.81	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	8 (5.6)	25 (9.0)
Number of Subjects Censored, n (%)	134 (94.4)	252 (91.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.180 (0.414)
95% CI		(0.524, 2.656)
Log-rank p-value		0.836

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.3 (90.4, 98.1)	92.7 (89.5, 95.8)
6 months	94.3 (90.4, 98.1)	88.9 (84.5, 93.4)
9 months	94.3 (90.4, 98.1)	87.4 (82.1, 92.7)
12 months	94.3 (90.4, 98.1)	87.4 (82.1, 92.7)
18 months	NE (NE, NE)	87.4 (82.1, 92.7)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	3 (2.1)	18 (6.5)
Number of Subjects Censored, n (%)	139 (97.9)	259 (93.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.606 (0.627)
95% CI		(0.762, 8.911)
Log-rank p-value		0.114

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (95.7, 100.0)	93.3 (90.2, 96.4)
6 months	94.1 (85.9, 100.0)	92.4 (88.8, 95.9)
9 months	94.1 (85.9, 100.0)	92.4 (88.8, 95.9)
12 months	94.1 (85.9, 100.0)	92.4 (88.8, 95.9)
18 months	NE (NE, NE)	92.4 (88.8, 95.9)
Median Follow-up Time (months)	2.81	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	7 (4.9)	14 (5.1)
Number of Subjects Censored, n (%)	135 (95.1)	263 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.848 (0.471)
95% CI		(0.337, 2.137)
Log-rank p-value		0.641

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (90.2, 98.5)	95.5 (93.0, 98.0)
6 months	94.4 (90.2, 98.5)	93.4 (89.6, 97.2)
9 months	94.4 (90.2, 98.5)	93.4 (89.6, 97.2)
12 months	94.4 (90.2, 98.5)	93.4 (89.6, 97.2)
18 months	NE (NE, NE)	93.4 (89.6, 97.2)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	2 (1.4)	22 (7.9)
Number of Subjects Censored, n (%)	140 (98.6)	255 (92.1)
Time to first TEAE (months)		
25% percentile (95% CI)	7.43 (7.43, NE)	NE (NE, NE)
Median (95% CI)	7.43 (7.43, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (7.43, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.491 (0.744)
95% CI		(1.045, 19.306)
Log-rank p-value		0.028

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	92.9 (89.7, 96.0)
6 months	99.3 (97.9, 100.0)	90.5 (86.5, 94.5)
9 months	NE (NE, NE)	90.5 (86.5, 94.5)
12 months	NE (NE, NE)	90.5 (86.5, 94.5)
18 months	NE (NE, NE)	90.5 (86.5, 94.5)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	2 (1.4)	13 (4.7)
Number of Subjects Censored, n (%)	140 (98.6)	264 (95.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.580 (0.766)
95% CI		(0.575, 11.569)
Log-rank p-value		0.198

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.6, 100.0)	95.5 (92.9, 98.1)
6 months	98.6 (96.6, 100.0)	94.8 (91.9, 97.7)
9 months	98.6 (96.6, 100.0)	93.6 (89.8, 97.3)
12 months	98.6 (96.6, 100.0)	93.6 (89.8, 97.3)
18 months	NE (NE, NE)	93.6 (89.8, 97.3)
Median Follow-up Time (months)	2.81	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	1 (0.7)	7 (2.5)
Number of Subjects Censored, n (%)	141 (99.3)	270 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.607 (1.078)
95% CI		(0.315, 21.556)
Log-rank p-value		0.372

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.8, 100.0)	97.5 (95.4, 99.5)
6 months	99.3 (97.8, 100.0)	96.6 (93.9, 99.2)
9 months	99.3 (97.8, 100.0)	96.6 (93.9, 99.2)
12 months	99.3 (97.8, 100.0)	96.6 (93.9, 99.2)
18 months	NE (NE, NE)	96.6 (93.9, 99.2)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	2 (1.4)	4 (1.4)
Number of Subjects Censored, n (%)	140 (98.6)	273 (98.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.875 (0.868)
95% CI		(0.160, 4.800)
Log-rank p-value		0.883

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (96.5, 100.0)	98.5 (97.0, 100.0)
6 months	98.5 (96.5, 100.0)	98.5 (97.0, 100.0)
9 months	98.5 (96.5, 100.0)	98.5 (97.0, 100.0)
12 months	98.5 (96.5, 100.0)	98.5 (97.0, 100.0)
18 months	NE (NE, NE)	98.5 (97.0, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	36 (25.4)	104 (37.5)
Number of Subjects Censored, n (%)	106 (74.6)	173 (62.5)
Time to first TEAE (months)		
25% percentile (95% CI)	2.53 (0.85, NE)	0.95 (0.69, 1.64)
Median (95% CI)	NE (NE, NE)	11.53 (6.41, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.389 (0.196)
95% CI		(0.947, 2.038)
Log-rank p-value		0.105

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	73.0 (65.3, 80.7)	66.7 (61.1, 72.3)
6 months	73.0 (65.3, 80.7)	59.9 (53.3, 66.6)
9 months	73.0 (65.3, 80.7)	57.4 (50.2, 64.6)
12 months	73.0 (65.3, 80.7)	43.2 (22.9, 63.6)
18 months	NE (NE, NE)	43.2 (22.9, 63.6)
Median Follow-up Time (months)	2.20	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	6 (4.2)	40 (14.4)
Number of Subjects Censored, n (%)	136 (95.8)	237 (85.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.583 (0.438)
95% CI		(1.518, 8.461)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.2 (91.4, 99.1)	85.7 (81.5, 89.9)
6 months	95.2 (91.4, 99.1)	85.1 (80.8, 89.4)
9 months	95.2 (91.4, 99.1)	85.1 (80.8, 89.4)
12 months	95.2 (91.4, 99.1)	85.1 (80.8, 89.4)
18 months	NE (NE, NE)	85.1 (80.8, 89.4)
Median Follow-up Time (months)	2.79	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	13 (9.2)	28 (10.1)
Number of Subjects Censored, n (%)	129 (90.8)	249 (89.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	14.32 (14.32, NE)
Median (95% CI)	NE (NE, NE)	NE (14.32, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.873 (0.345)
95% CI		(0.444, 1.717)
Log-rank p-value		0.679

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.7 (85.9, 95.5)	91.9 (88.6, 95.1)
6 months	90.7 (85.9, 95.5)	88.6 (84.0, 93.1)
9 months	90.7 (85.9, 95.5)	87.3 (82.3, 92.4)
12 months	90.7 (85.9, 95.5)	87.3 (82.3, 92.4)
18 months	NE (NE, NE)	69.9 (39.0, 100.0)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	14 (9.9)	21 (7.6)
Number of Subjects Censored, n (%)	128 (90.1)	256 (92.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.584 (0.357)
95% CI		(0.290, 1.176)
Log-rank p-value		0.114

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.6 (84.4, 94.8)	93.8 (90.9, 96.6)
6 months	89.6 (84.4, 94.8)	92.3 (88.8, 95.8)
9 months	89.6 (84.4, 94.8)	90.9 (86.6, 95.3)
12 months	89.6 (84.4, 94.8)	80.8 (61.8, 99.9)
18 months	NE (NE, NE)	80.8 (61.8, 99.9)
Median Follow-up Time (months)	2.55	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	2 (1.4)	11 (4.0)
Number of Subjects Censored, n (%)	140 (98.6)	266 (96.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.649 (0.769)
95% CI		(0.586, 11.962)
Log-rank p-value		0.208

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.6, 100.0)	95.9 (93.5, 98.3)
6 months	98.6 (96.6, 100.0)	95.9 (93.5, 98.3)
9 months	98.6 (96.6, 100.0)	95.9 (93.5, 98.3)
12 months	98.6 (96.6, 100.0)	95.9 (93.5, 98.3)
18 months	NE (NE, NE)	95.9 (93.5, 98.3)
Median Follow-up Time (months)	2.81	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	1 (0.7)	8 (2.9)
Number of Subjects Censored, n (%)	141 (99.3)	269 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.794 (1.082)
95% CI		(0.335, 23.272)
Log-rank p-value		0.330

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	98.2 (96.6, 99.8)
6 months	99.3 (97.9, 100.0)	97.2 (94.7, 99.7)
9 months	99.3 (97.9, 100.0)	94.0 (89.0, 99.0)
12 months	99.3 (97.9, 100.0)	94.0 (89.0, 99.0)
18 months	NE (NE, NE)	94.0 (89.0, 99.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Vascular disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	20 (14.1)	109 (39.4)
Number of Subjects Censored, n (%)	122 (85.9)	168 (60.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.92 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	NE (6.44, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.929 (0.245)
95% CI		(1.814, 4.731)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Vascular disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.3 (79.3, 91.3)	61.0 (55.0, 67.0)
6 months	85.3 (79.3, 91.3)	57.8 (51.3, 64.3)
9 months	NE (NE, NE)	54.4 (46.8, 62.1)
12 months	NE (NE, NE)	54.4 (46.8, 62.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.55	2.66

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	11 (7.7)	100 (36.1)
Number of Subjects Censored, n (%)	131 (92.3)	177 (63.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.02 (0.69, 2.07)
Median (95% CI)	NE (NE, NE)	NE (7.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.909 (0.319)
95% CI		(2.628, 9.172)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.0 (87.4, 96.5)	64.5 (58.6, 70.3)
6 months	92.0 (87.4, 96.5)	62.3 (56.2, 68.5)
9 months	NE (NE, NE)	57.2 (49.2, 65.1)
12 months	NE (NE, NE)	57.2 (49.2, 65.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.73	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	21 (14.8)	88 (31.8)
Number of Subjects Censored, n (%)	121 (85.2)	189 (68.2)
Time to first TEAE (months)		
25% percentile (95% CI)	5.59 (5.59, NE)	1.84 (1.22, 4.04)
Median (95% CI)	NE (5.59, NE)	NE (8.64, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.962 (0.246)
95% CI		(1.212, 3.175)
Log-rank p-value		0.006

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.3 (79.3, 91.3)	70.3 (64.8, 75.9)
6 months	71.1 (45.2, 97.0)	65.6 (59.0, 72.2)
9 months	NE (NE, NE)	59.2 (49.8, 68.5)
12 months	NE (NE, NE)	55.2 (43.7, 66.7)
18 months	NE (NE, NE)	55.2 (43.7, 66.7)
Median Follow-up Time (months)	2.46	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	8 (5.6)	29 (10.5)
Number of Subjects Censored, n (%)	134 (94.4)	248 (89.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.499 (0.405)
95% CI		(0.678, 3.317)
Log-rank p-value		0.294

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.1 (90.1, 98.1)	91.1 (87.6, 94.6)
6 months	94.1 (90.1, 98.1)	87.1 (82.2, 92.0)
9 months	94.1 (90.1, 98.1)	85.8 (80.4, 91.2)
12 months	94.1 (90.1, 98.1)	85.8 (80.4, 91.2)
18 months	NE (NE, NE)	85.8 (80.4, 91.2)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	5 (3.5)	24 (8.7)
Number of Subjects Censored, n (%)	137 (96.5)	253 (91.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.958 (0.501)
95% CI		(0.734, 5.222)
Log-rank p-value		0.179

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.0 (94.1, 99.9)	92.1 (88.8, 95.3)
6 months	84.9 (62.5, 100.0)	91.3 (87.8, 94.9)
9 months	NE (NE, NE)	87.7 (81.8, 93.7)
12 months	NE (NE, NE)	87.7 (81.8, 93.7)
18 months	NE (NE, NE)	87.7 (81.8, 93.7)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	1 (0.7)	19 (6.9)
Number of Subjects Censored, n (%)	141 (99.3)	258 (93.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		8.654 (1.029)
95% CI		(1.153, 64.977)
Log-rank p-value		0.011

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.3, 100.0)	93.2 (90.2, 96.3)
6 months	99.1 (97.3, 100.0)	92.2 (88.6, 95.8)
9 months	99.1 (97.3, 100.0)	92.2 (88.6, 95.8)
12 months	99.1 (97.3, 100.0)	92.2 (88.6, 95.8)
18 months	NE (NE, NE)	92.2 (88.6, 95.8)
Median Follow-up Time (months)	2.81	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	3 (2.1)	8 (2.9)
Number of Subjects Censored, n (%)	139 (97.9)	269 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.165 (0.685)
95% CI		(0.304, 4.463)
Log-rank p-value		0.829

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.3, 100.0)	97.4 (95.5, 99.3)
6 months	97.8 (95.3, 100.0)	96.2 (93.1, 99.2)
9 months	97.8 (95.3, 100.0)	96.2 (93.1, 99.2)
12 months	97.8 (95.3, 100.0)	96.2 (93.1, 99.2)
18 months	NE (NE, NE)	96.2 (93.1, 99.2)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	1 (0.7)	10 (3.6)
Number of Subjects Censored, n (%)	141 (99.3)	267 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.365 (1.070)
95% CI		(0.413, 27.429)
Log-rank p-value		0.226

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	97.8 (96.0, 99.5)
6 months	99.3 (97.9, 100.0)	96.7 (93.9, 99.4)
9 months	99.3 (97.9, 100.0)	89.8 (81.7, 98.0)
12 months	99.3 (97.9, 100.0)	89.8 (81.7, 98.0)
18 months	NE (NE, NE)	89.8 (81.7, 98.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	0	8 (2.9)
Number of Subjects Censored, n (%)	142 (100.0)	269 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.049

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.9 (94.8, 99.0)
6 months	100.0 (100.0, 100.0)	96.9 (94.8, 99.0)
9 months	100.0 (100.0, 100.0)	96.9 (94.8, 99.0)
12 months	100.0 (100.0, 100.0)	96.9 (94.8, 99.0)
18 months	NE (NE, NE)	96.9 (94.8, 99.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	17 (12.0)	95 (34.3)
Number of Subjects Censored, n (%)	125 (88.0)	182 (65.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	1.58 (0.72, 2.33)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.840 (0.265)
95% CI		(1.691, 4.770)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.4 (83.0, 93.7)	67.5 (61.8, 73.1)
6 months	83.9 (74.1, 93.8)	62.6 (56.1, 69.1)
9 months	83.9 (74.1, 93.8)	58.9 (50.8, 66.9)
12 months	83.9 (74.1, 93.8)	58.9 (50.8, 66.9)
18 months	NE (NE, NE)	58.9 (50.8, 66.9)
Median Follow-up Time (months)	2.61	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	3 (2.1)	55 (19.9)
Number of Subjects Censored, n (%)	139 (97.9)	222 (80.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	7.39 (3.84, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		8.771 (0.594)
95% CI		(2.739, 28.088)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.9 (95.5, 100.0)	82.3 (77.7, 86.8)
6 months	97.9 (95.5, 100.0)	77.1 (71.1, 83.0)
9 months	97.9 (95.5, 100.0)	74.9 (67.7, 82.0)
12 months	97.9 (95.5, 100.0)	74.9 (67.7, 82.0)
18 months	NE (NE, NE)	74.9 (67.7, 82.0)
Median Follow-up Time (months)	2.79	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	4 (2.8)	11 (4.0)
Number of Subjects Censored, n (%)	138 (97.2)	266 (96.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.304 (0.586)
95% CI		(0.413, 4.114)
Log-rank p-value		0.702

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.1 (94.4, 99.9)	95.8 (93.3, 98.2)
6 months	97.1 (94.4, 99.9)	95.8 (93.3, 98.2)
9 months	97.1 (94.4, 99.9)	95.8 (93.3, 98.2)
12 months	97.1 (94.4, 99.9)	95.8 (93.3, 98.2)
18 months	NE (NE, NE)	95.8 (93.3, 98.2)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	3 (2.1)	7 (2.5)
Number of Subjects Censored, n (%)	139 (97.9)	270 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.108 (0.694)
95% CI		(0.284, 4.320)
Log-rank p-value		0.992

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.4 (96.3, 100.0)	97.4 (95.4, 99.3)
6 months	94.3 (86.2, 100.0)	97.4 (95.4, 99.3)
9 months	94.3 (86.2, 100.0)	97.4 (95.4, 99.3)
12 months	94.3 (86.2, 100.0)	97.4 (95.4, 99.3)
18 months	NE (NE, NE)	97.4 (95.4, 99.3)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Nervous system disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	26 (18.3)	70 (25.3)
Number of Subjects Censored, n (%)	116 (81.7)	207 (74.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.87, NE)	4.14 (1.84, NE)
Median (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.190 (0.233)
95% CI		(0.754, 1.877)
Log-rank p-value		0.505

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Nervous system disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.2 (73.3, 87.2)	77.6 (72.6, 82.6)
6 months	80.2 (73.3, 87.2)	71.1 (64.7, 77.5)
9 months	80.2 (73.3, 87.2)	69.8 (63.1, 76.6)
12 months	80.2 (73.3, 87.2)	69.8 (63.1, 76.6)
18 months	NE (NE, NE)	69.8 (63.1, 76.6)
Median Follow-up Time (months)	2.32	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	7 (4.9)	27 (9.7)
Number of Subjects Censored, n (%)	135 (95.1)	250 (90.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	18.04 (18.04, NE)
Median (95% CI)	NE (NE, NE)	NE (18.04, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (18.04, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.745 (0.429)
95% CI		(0.753, 4.042)
Log-rank p-value		0.183

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.2 (89.9, 98.5)	91.5 (88.2, 94.8)
6 months	94.2 (89.9, 98.5)	89.8 (85.7, 93.8)
9 months	94.2 (89.9, 98.5)	88.4 (83.7, 93.2)
12 months	94.2 (89.9, 98.5)	88.4 (83.7, 93.2)
18 months	NE (NE, NE)	88.4 (83.7, 93.2)
Median Follow-up Time (months)	2.79	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	6 (4.2)	5 (1.8)
Number of Subjects Censored, n (%)	136 (95.8)	272 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.389 (0.608)
95% CI		(0.118, 1.281)
Log-rank p-value		0.101

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (92.3, 99.1)	98.1 (96.4, 99.8)
6 months	95.7 (92.3, 99.1)	98.1 (96.4, 99.8)
9 months	95.7 (92.3, 99.1)	98.1 (96.4, 99.8)
12 months	95.7 (92.3, 99.1)	98.1 (96.4, 99.8)
18 months	NE (NE, NE)	98.1 (96.4, 99.8)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	3 (2.1)	10 (3.6)
Number of Subjects Censored, n (%)	139 (97.9)	267 (96.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.681 (0.659)
95% CI		(0.462, 6.115)
Log-rank p-value		0.418

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (95.2, 100.0)	96.3 (94.0, 98.5)
6 months	97.7 (95.2, 100.0)	96.3 (94.0, 98.5)
9 months	97.7 (95.2, 100.0)	96.3 (94.0, 98.5)
12 months	97.7 (95.2, 100.0)	96.3 (94.0, 98.5)
18 months	NE (NE, NE)	96.3 (94.0, 98.5)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	18 (12.7)	68 (24.5)
Number of Subjects Censored, n (%)	124 (87.3)	209 (75.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	4.57 (2.46, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.645 (0.268)
95% CI		(0.972, 2.783)
Log-rank p-value		0.067

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.5 (80.4, 92.7)	76.5 (71.3, 81.7)
6 months	82.4 (72.6, 92.2)	72.3 (66.1, 78.4)
9 months	82.4 (72.6, 92.2)	69.2 (61.9, 76.4)
12 months	82.4 (72.6, 92.2)	69.2 (61.9, 76.4)
18 months	NE (NE, NE)	69.2 (61.9, 76.4)
Median Follow-up Time (months)	2.66	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	6 (4.2)	52 (18.8)
Number of Subjects Censored, n (%)	136 (95.8)	225 (81.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.02, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.047 (0.433)
95% CI		(1.733, 9.455)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.7 (92.3, 99.1)	80.6 (75.7, 85.5)
6 months	95.7 (92.3, 99.1)	79.1 (73.9, 84.3)
9 months	95.7 (92.3, 99.1)	79.1 (73.9, 84.3)
12 months	95.7 (92.3, 99.1)	79.1 (73.9, 84.3)
18 months	NE (NE, NE)	79.1 (73.9, 84.3)
Median Follow-up Time (months)	2.79	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	3 (2.1)	4 (1.4)
Number of Subjects Censored, n (%)	139 (97.9)	273 (98.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.592 (0.772)
95% CI		(0.130, 2.689)
Log-rank p-value		0.534

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (95.0, 100.0)	98.5 (97.1, 100.0)
6 months	97.7 (95.0, 100.0)	98.5 (97.1, 100.0)
9 months	97.7 (95.0, 100.0)	98.5 (97.1, 100.0)
12 months	97.7 (95.0, 100.0)	98.5 (97.1, 100.0)
18 months	NE (NE, NE)	98.5 (97.1, 100.0)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Infections and infestations**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	17 (12.0)	52 (18.8)
Number of Subjects Censored, n (%)	125 (88.0)	225 (81.2)
Time to first TEAE (months)		
25% percentile (95% CI)	5.78 (4.34, NE)	6.54 (5.52, 17.48)
Median (95% CI)	NE (5.78, NE)	17.48 (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.48, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.069 (0.289)
95% CI		(0.606, 1.884)
Log-rank p-value		0.766

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Infections and infestations**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.1 (83.9, 94.3)	86.3 (82.1, 90.5)
6 months	66.5 (35.8, 97.3)	77.3 (70.7, 84.0)
9 months	66.5 (35.8, 97.3)	70.4 (61.5, 79.4)
12 months	66.5 (35.8, 97.3)	62.6 (46.1, 79.1)
18 months	NE (NE, NE)	47.0 (17.7, 76.3)
Median Follow-up Time (months)	2.73	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	5 (3.5)	11 (4.0)
Number of Subjects Censored, n (%)	137 (96.5)	266 (96.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.659 (0.578)
95% CI		(0.213, 2.046)
Log-rank p-value		0.403

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (94.4, 99.9)	97.4 (95.5, 99.3)
6 months	91.8 (81.2, 100.0)	94.4 (90.4, 98.3)
9 months	91.8 (81.2, 100.0)	93.0 (88.4, 97.7)
12 months	91.8 (81.2, 100.0)	93.0 (88.4, 97.7)
18 months	NE (NE, NE)	93.0 (88.4, 97.7)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	2 (1.4)	8 (2.9)
Number of Subjects Censored, n (%)	140 (98.6)	269 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (11.56, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.857 (0.830)
95% CI		(0.168, 4.360)
Log-rank p-value		0.822

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	98.7 (97.3, 100.0)
6 months	93.4 (82.3, 100.0)	96.6 (93.8, 99.4)
9 months	93.4 (82.3, 100.0)	95.0 (90.9, 99.1)
12 months	93.4 (82.3, 100.0)	85.5 (67.5, 100.0)
18 months	NE (NE, NE)	85.5 (67.5, 100.0)
Median Follow-up Time (months)	2.81	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	1 (0.7)	8 (2.9)
Number of Subjects Censored, n (%)	141 (99.3)	269 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.592 (1.077)
95% CI		(0.314, 21.401)
Log-rank p-value		0.397

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	97.1 (95.0, 99.3)
6 months	99.3 (97.9, 100.0)	96.0 (93.0, 99.0)
9 months	99.3 (97.9, 100.0)	96.0 (93.0, 99.0)
12 months	99.3 (97.9, 100.0)	96.0 (93.0, 99.0)
18 months	NE (NE, NE)	96.0 (93.0, 99.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	20 (14.1)	37 (13.4)
Number of Subjects Censored, n (%)	122 (85.9)	240 (86.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.802 (0.283)
95% CI		(0.461, 1.395)
Log-rank p-value		0.458

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.0 (78.8, 91.1)	86.8 (82.6, 90.9)
6 months	85.0 (78.8, 91.1)	83.8 (78.5, 89.1)
9 months	85.0 (78.8, 91.1)	83.8 (78.5, 89.1)
12 months	85.0 (78.8, 91.1)	83.8 (78.5, 89.1)
18 months	NE (NE, NE)	83.8 (78.5, 89.1)
Median Follow-up Time (months)	2.58	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	13 (9.2)	22 (7.9)
Number of Subjects Censored, n (%)	129 (90.8)	255 (92.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	17.74 (17.74, NE)
Median (95% CI)	NE (NE, NE)	NE (17.74, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.74, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.649 (0.363)
95% CI		(0.319, 1.321)
Log-rank p-value		0.250

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.1 (85.0, 95.2)	93.0 (89.8, 96.1)
6 months	90.1 (85.0, 95.2)	90.1 (85.7, 94.6)
9 months	90.1 (85.0, 95.2)	90.1 (85.7, 94.6)
12 months	90.1 (85.0, 95.2)	90.1 (85.7, 94.6)
18 months	NE (NE, NE)	60.1 (11.9, 100.0)
Median Follow-up Time (months)	2.66	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	1 (0.7)	17 (6.1)
Number of Subjects Censored, n (%)	141 (99.3)	260 (93.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		8.562 (1.030)
95% CI		(1.138, 64.437)
Log-rank p-value		0.013

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	93.4 (90.3, 96.5)
6 months	99.3 (97.9, 100.0)	93.4 (90.3, 96.5)
9 months	99.3 (97.9, 100.0)	93.4 (90.3, 96.5)
12 months	99.3 (97.9, 100.0)	93.4 (90.3, 96.5)
18 months	NE (NE, NE)	93.4 (90.3, 96.5)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Endocrine disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	1 (0.7)	59 (21.3)
Number of Subjects Censored, n (%)	141 (99.3)	218 (78.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.52 (3.81, 6.90)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6, 12.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		22.881 (1.010)
95% CI		(3.160, 165.699)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Endocrine disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	84.4 (79.9, 88.9)
6 months	99.3 (97.9, 100.0)	69.2 (61.4, 77.0)
9 months	99.3 (97.9, 100.0)	65.9 (57.2, 74.5)
12 months	99.3 (97.9, 100.0)	65.9 (57.2, 74.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	1 (0.7)	58 (20.9)
Number of Subjects Censored, n (%)	141 (99.3)	219 (79.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.59 (3.81, 7.33)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6, 12.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		22.171 (1.010)
95% CI		(3.060, 160.660)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	84.8 (80.4, 89.2)
6 months	99.3 (97.9, 100.0)	70.6 (63.0, 78.2)
9 months	99.3 (97.9, 100.0)	65.2 (56.0, 74.4)
12 months	99.3 (97.9, 100.0)	65.2 (56.0, 74.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Psychiatric disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	10 (7.0)	31 (11.2)
Number of Subjects Censored, n (%)	132 (93.0)	246 (88.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.228 (0.370)
95% CI		(0.594, 2.538)
Log-rank p-value		0.638

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Psychiatric disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.6 (88.2, 97.1)	90.3 (86.7, 94.0)
6 months	92.6 (88.2, 97.1)	85.3 (80.1, 90.6)
9 months	92.6 (88.2, 97.1)	85.3 (80.1, 90.6)
12 months	92.6 (88.2, 97.1)	85.3 (80.1, 90.6)
18 months	NE (NE, NE)	85.3 (80.1, 90.6)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	8 (5.6)	11 (4.0)
Number of Subjects Censored, n (%)	134 (94.4)	266 (96.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.533 (0.473)
95% CI		(0.211, 1.346)
Log-rank p-value		0.144

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.1 (90.1, 98.1)	96.3 (94.0, 98.7)
6 months	94.1 (90.1, 98.1)	94.7 (91.4, 98.0)
9 months	94.1 (90.1, 98.1)	94.7 (91.4, 98.0)
12 months	94.1 (90.1, 98.1)	94.7 (91.4, 98.0)
18 months	NE (NE, NE)	94.7 (91.4, 98.0)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	0	5 (1.8)
Number of Subjects Censored, n (%)	142 (100.0)	272 (98.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.168

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.1 (96.4, 99.7)
6 months	100.0 (100.0, 100.0)	98.1 (96.4, 99.7)
9 months	100.0 (100.0, 100.0)	98.1 (96.4, 99.7)
12 months	100.0 (100.0, 100.0)	98.1 (96.4, 99.7)
18 months	NE (NE, NE)	98.1 (96.4, 99.7)
Median Follow-up Time (months)	2.83	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	0	11 (4.0)
Number of Subjects Censored, n (%)	142 (100.0)	266 (96.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.045

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.5 (94.3, 98.8)
6 months	100.0 (100.0, 100.0)	94.8 (91.6, 98.1)
9 months	100.0 (100.0, 100.0)	94.8 (91.6, 98.1)
12 months	100.0 (100.0, 100.0)	94.8 (91.6, 98.1)
18 months	NE (NE, NE)	94.8 (91.6, 98.1)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	11 (7.7)	26 (9.4)
Number of Subjects Censored, n (%)	131 (92.3)	251 (90.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.66, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.873 (0.369)
95% CI		(0.424, 1.801)
Log-rank p-value		0.754

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.0 (87.5, 96.5)	92.4 (89.1, 95.7)
6 months	92.0 (87.5, 96.5)	88.3 (83.4, 93.1)
9 months	92.0 (87.5, 96.5)	86.3 (80.1, 92.4)
12 months	92.0 (87.5, 96.5)	82.5 (73.2, 91.8)
18 months	NE (NE, NE)	82.5 (73.2, 91.8)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	1 (0.7)	11 (4.0)
Number of Subjects Censored, n (%)	141 (99.3)	266 (96.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.153 (1.052)
95% CI		(0.529, 32.621)
Log-rank p-value		0.156

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	96.3 (93.9, 98.7)
6 months	99.3 (97.9, 100.0)	95.6 (92.8, 98.3)
9 months	99.3 (97.9, 100.0)	95.6 (92.8, 98.3)
12 months	99.3 (97.9, 100.0)	91.4 (83.0, 99.8)
18 months	NE (NE, NE)	91.4 (83.0, 99.8)
Median Follow-up Time (months)	2.81	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3M
Summary of Time to Onset of TEAE by SOC/PT by Prior EGFRi
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
No

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Number of Subjects with Events, n (%)	1 (0.7)	8 (2.9)
Number of Subjects Censored, n (%)	141 (99.3)	269 (97.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 13.0*	0.6*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.183 (1.083)
95% CI		(0.261, 18.244)
Log-rank p-value		0.454

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
TAS-102

Statistics	Placebo + BSC N=142	Fruquintinib + BSC N=277
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (97.9, 100.0)	98.0 (96.3, 99.7)
6 months	99.3 (97.9, 100.0)	96.2 (93.2, 99.2)
9 months	99.3 (97.9, 100.0)	94.2 (89.3, 99.1)
12 months	99.3 (97.9, 100.0)	94.2 (89.3, 99.1)
18 months	NE (NE, NE)	94.2 (89.3, 99.1)
Median Follow-up Time (months)	2.83	3.75

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	67 (55.4)	168 (70.9)
Number of Subjects Censored, n (%)	54 (44.6)	69 (29.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.49, 0.76)	0.30 (0.20, 0.66)
Median (95% CI)	1.87 (1.28, 3.71)	0.95 (0.69, 1.51)
75% percentile (95% CI)	NE (NE, NE)	5.59 (3.75, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Min, Max	0.0, 13.0*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.416 (0.146)
95% CI		(1.065, 1.884)
Log-rank p-value		0.021

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	44.3 (35.2, 53.5)	34.1 (28.0, 40.2)
6 months	39.1 (28.3, 49.8)	24.7 (18.0, 31.3)
9 months	39.1 (28.3, 49.8)	19.6 (12.2, 26.9)
12 months	39.1 (28.3, 49.8)	19.6 (12.2, 26.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.68	0.95

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	25 (20.7)	88 (37.1)
Number of Subjects Censored, n (%)	96 (79.3)	149 (62.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.28, NE)	0.92 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.865 (0.227)
95% CI		(1.195, 2.911)
Log-rank p-value		0.006

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	78.1 (70.3, 85.8)	63.2 (57.0, 69.5)
6 months	78.1 (70.3, 85.8)	61.9 (55.5, 68.3)
9 months	78.1 (70.3, 85.8)	59.5 (51.8, 67.2)
12 months	78.1 (70.3, 85.8)	59.5 (51.8, 67.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.53	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	21 (17.4)	49 (20.7)
Number of Subjects Censored, n (%)	100 (82.6)	188 (79.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.97, NE)	7.29 (3.68, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.069 (0.264)
95% CI		(0.637, 1.792)
Log-rank p-value		0.812

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.6 (74.4, 88.8)	81.4 (76.3, 86.4)
6 months	81.6 (74.4, 88.8)	77.6 (71.5, 83.7)
9 months	81.6 (74.4, 88.8)	74.3 (67.0, 81.6)
12 months	81.6 (74.4, 88.8)	74.3 (67.0, 81.6)
18 months	NE (NE, NE)	74.3 (67.0, 81.6)
Median Follow-up Time (months)	2.60	3.09

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	8 (6.6)	19 (8.0)
Number of Subjects Censored, n (%)	113 (93.4)	218 (92.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.166 (0.423)
95% CI		(0.509, 2.673)
Log-rank p-value		0.728

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.1 (88.6, 97.7)	92.1 (88.6, 95.6)
6 months	93.1 (88.6, 97.7)	91.2 (87.2, 95.1)
9 months	93.1 (88.6, 97.7)	91.2 (87.2, 95.1)
12 months	93.1 (88.6, 97.7)	91.2 (87.2, 95.1)
18 months	NE (NE, NE)	91.2 (87.2, 95.1)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	4 (3.3)	42 (17.7)
Number of Subjects Censored, n (%)	117 (96.7)	195 (82.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.67, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.278 (0.525)
95% CI		(1.887, 14.760)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.6 (93.3, 99.9)	83.7 (78.9, 88.4)
6 months	96.6 (93.3, 99.9)	82.0 (76.8, 87.2)
9 months	96.6 (93.3, 99.9)	78.1 (70.9, 85.4)
12 months	96.6 (93.3, 99.9)	78.1 (70.9, 85.4)
18 months	NE (NE, NE)	78.1 (70.9, 85.4)
Median Follow-up Time (months)	2.83	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	16 (13.2)	13 (5.5)
Number of Subjects Censored, n (%)	105 (86.8)	224 (94.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.19, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.321 (0.379)
95% CI		(0.153, 0.676)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.6 (78.7, 92.4)	95.5 (92.8, 98.3)
6 months	83.2 (75.2, 91.3)	93.0 (89.1, 96.9)
9 months	83.2 (75.2, 91.3)	93.0 (89.1, 96.9)
12 months	83.2 (75.2, 91.3)	93.0 (89.1, 96.9)
18 months	NE (NE, NE)	93.0 (89.1, 96.9)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	7 (5.8)	12 (5.1)
Number of Subjects Censored, n (%)	114 (94.2)	225 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.792 (0.482)
95% CI		(0.308, 2.037)
Log-rank p-value		0.619

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.6 (88.9, 98.3)	95.2 (92.4, 98.0)
6 months	93.6 (88.9, 98.3)	95.2 (92.4, 98.0)
9 months	93.6 (88.9, 98.3)	91.9 (85.1, 98.8)
12 months	93.6 (88.9, 98.3)	91.9 (85.1, 98.8)
18 months	NE (NE, NE)	91.9 (85.1, 98.8)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	4 (3.3)	6 (2.5)
Number of Subjects Censored, n (%)	117 (96.7)	231 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.82, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.402 (0.716)
95% CI		(0.099, 1.638)
Log-rank p-value		0.176

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.5 (93.0, 99.9)	98.7 (97.2, 100.0)
6 months	96.5 (93.0, 99.9)	98.7 (97.2, 100.0)
9 months	96.5 (93.0, 99.9)	96.6 (92.4, 100.0)
12 months	96.5 (93.0, 99.9)	88.5 (76.9, 100.0)
18 months	NE (NE, NE)	88.5 (76.9, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	1 (0.8)	5 (2.1)
Number of Subjects Censored, n (%)	120 (99.2)	232 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.354 (1.128)
95% CI		(0.148, 12.353)
Log-rank p-value		0.807

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.5 (95.6, 100.0)	98.5 (96.7, 100.0)
6 months	98.5 (95.6, 100.0)	97.5 (95.0, 100.0)
9 months	98.5 (95.6, 100.0)	95.5 (91.0, 100.0)
12 months	98.5 (95.6, 100.0)	95.5 (91.0, 100.0)
18 months	NE (NE, NE)	95.5 (91.0, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	2 (1.7)	6 (2.5)
Number of Subjects Censored, n (%)	119 (98.3)	231 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.361 (0.830)
95% CI		(0.267, 6.928)
Log-rank p-value		0.710

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (96.0, 100.0)	97.9 (96.0, 99.7)
6 months	98.3 (96.0, 100.0)	97.9 (96.0, 99.7)
9 months	98.3 (96.0, 100.0)	95.1 (89.4, 100.0)
12 months	98.3 (96.0, 100.0)	95.1 (89.4, 100.0)
18 months	NE (NE, NE)	95.1 (89.4, 100.0)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	71 (58.7)	161 (67.9)
Number of Subjects Censored, n (%)	50 (41.3)	76 (32.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.53 (0.16, 0.69)	0.59 (0.43, 0.69)
Median (95% CI)	1.45 (0.95, 2.07)	1.61 (0.95, 2.20)
75% percentile (95% CI)	5.59 (5.59, NE)	6.70 (5.03, NE)
Min, Max	0.0, 5.6*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.999 (0.145)
95% CI		(0.752, 1.328)
Log-rank p-value		0.989

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	40.8 (31.7, 49.9)	37.8 (31.5, 44.2)
6 months	NE (NE, NE)	27.9 (20.8, 35.0)
9 months	NE (NE, NE)	19.7 (11.8, 27.6)
12 months	NE (NE, NE)	14.8 (4.5, 25.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.38	1.45

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	9 (7.4)	58 (24.5)
Number of Subjects Censored, n (%)	112 (92.6)	179 (75.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.96 (2.37, 7.33)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.940 (0.361)
95% CI		(1.449, 5.967)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.5 (87.8, 97.2)	79.6 (74.3, 84.8)
6 months	92.5 (87.8, 97.2)	70.1 (62.4, 77.7)
9 months	92.5 (87.8, 97.2)	66.8 (58.3, 75.4)
12 months	92.5 (87.8, 97.2)	66.8 (58.3, 75.4)
18 months	NE (NE, NE)	66.8 (58.3, 75.4)
Median Follow-up Time (months)	2.79	2.89

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	21 (17.4)	40 (16.9)
Number of Subjects Censored, n (%)	100 (82.6)	197 (83.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.91, NE)	9.00 (5.55, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.706 (0.278)
95% CI		(0.410, 1.217)
Log-rank p-value		0.168

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.2 (75.2, 89.1)	86.6 (82.2, 91.1)
6 months	82.2 (75.2, 89.1)	80.7 (74.1, 87.3)
9 months	82.2 (75.2, 89.1)	76.0 (67.9, 84.1)
12 months	82.2 (75.2, 89.1)	69.5 (58.2, 80.9)
18 months	NE (NE, NE)	69.5 (58.2, 80.9)
Median Follow-up Time (months)	2.63	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	20 (16.5)	45 (19.0)
Number of Subjects Censored, n (%)	101 (83.5)	192 (81.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.53, NE)	9.23 (5.52, NE)
Median (95% CI)	NE (NE, NE)	NE (12.25, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (12.25, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.892 (0.275)
95% CI		(0.520, 1.530)
Log-rank p-value		0.711

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.0 (75.9, 90.0)	83.1 (78.1, 88.0)
6 months	76.1 (61.6, 90.6)	81.0 (75.4, 86.7)
9 months	76.1 (61.6, 90.6)	77.9 (71.0, 84.8)
12 months	76.1 (61.6, 90.6)	69.7 (57.0, 82.4)
18 months	NE (NE, NE)	52.3 (21.2, 83.3)
Median Follow-up Time (months)	2.76	3.29

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	14 (11.6)	34 (14.3)
Number of Subjects Censored, n (%)	107 (88.4)	203 (85.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.70, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.974 (0.323)
95% CI		(0.517, 1.833)
Log-rank p-value		0.885

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.8 (83.0, 94.6)	87.3 (82.9, 91.8)
6 months	86.1 (78.6, 93.7)	82.9 (77.1, 88.6)
9 months	86.1 (78.6, 93.7)	81.3 (74.9, 87.7)
12 months	86.1 (78.6, 93.7)	81.3 (74.9, 87.7)
18 months	NE (NE, NE)	81.3 (74.9, 87.7)
Median Follow-up Time (months)	2.83	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	14 (11.6)	33 (13.9)
Number of Subjects Censored, n (%)	107 (88.4)	204 (86.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.52, NE)	NE (7.10, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.969 (0.327)
95% CI		(0.511, 1.839)
Log-rank p-value		0.908

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.8 (83.1, 94.6)	88.7 (84.7, 92.8)
6 months	85.0 (75.8, 94.2)	85.9 (80.8, 91.1)
9 months	85.0 (75.8, 94.2)	81.0 (73.6, 88.3)
12 months	85.0 (75.8, 94.2)	77.4 (67.7, 87.2)
18 months	NE (NE, NE)	77.4 (67.7, 87.2)
Median Follow-up Time (months)	2.83	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	3 (2.5)	24 (10.1)
Number of Subjects Censored, n (%)	118 (97.5)	213 (89.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.619 (0.616)
95% CI		(1.083, 12.097)
Log-rank p-value		0.027

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (94.2, 100.0)	91.5 (87.9, 95.1)
6 months	97.3 (94.2, 100.0)	88.9 (84.4, 93.4)
9 months	97.3 (94.2, 100.0)	87.3 (81.8, 92.7)
12 months	97.3 (94.2, 100.0)	87.3 (81.8, 92.7)
18 months	NE (NE, NE)	87.3 (81.8, 92.7)
Median Follow-up Time (months)	2.83	3.48

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	3 (2.5)	20 (8.4)
Number of Subjects Censored, n (%)	118 (97.5)	217 (91.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.856 (0.625)
95% CI		(0.839, 9.724)
Log-rank p-value		0.088

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (96.1, 100.0)	92.5 (89.0, 95.9)
6 months	87.4 (67.1, 100.0)	90.3 (85.8, 94.9)
9 months	NE (NE, NE)	88.3 (82.3, 94.2)
12 months	NE (NE, NE)	88.3 (82.3, 94.2)
18 months	NE (NE, NE)	88.3 (82.3, 94.2)
Median Follow-up Time (months)	2.83	3.42

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	4 (3.3)	8 (3.4)
Number of Subjects Censored, n (%)	117 (96.7)	229 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.897 (0.625)
95% CI		(0.264, 3.052)
Log-rank p-value		0.864

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.5 (93.1, 99.9)	97.0 (94.9, 99.2)
6 months	96.5 (93.1, 99.9)	97.0 (94.9, 99.2)
9 months	96.5 (93.1, 99.9)	95.1 (90.9, 99.4)
12 months	96.5 (93.1, 99.9)	95.1 (90.9, 99.4)
18 months	NE (NE, NE)	95.1 (90.9, 99.4)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	1 (0.8)	6 (2.5)
Number of Subjects Censored, n (%)	120 (99.2)	231 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.654 (1.083)
95% CI		(0.318, 22.155)
Log-rank p-value		0.349

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.5, 100.0)	97.2 (95.0, 99.5)
6 months	99.2 (97.5, 100.0)	97.2 (95.0, 99.5)
9 months	99.2 (97.5, 100.0)	97.2 (95.0, 99.5)
12 months	99.2 (97.5, 100.0)	97.2 (95.0, 99.5)
18 months	NE (NE, NE)	97.2 (95.0, 99.5)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	6 (5.0)	2 (0.8)
Number of Subjects Censored, n (%)	115 (95.0)	235 (99.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.113 (0.873)
95% CI		(0.021, 0.628)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.7 (90.5, 98.8)	99.6 (98.7, 100.0)
6 months	94.7 (90.5, 98.8)	98.2 (95.5, 100.0)
9 months	94.7 (90.5, 98.8)	98.2 (95.5, 100.0)
12 months	94.7 (90.5, 98.8)	98.2 (95.5, 100.0)
18 months	NE (NE, NE)	98.2 (95.5, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	0	7 (3.0)
Number of Subjects Censored, n (%)	121 (100.0)	230 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.086

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.4 (95.3, 99.4)
6 months	100.0 (100.0, 100.0)	97.4 (95.3, 99.4)
9 months	100.0 (100.0, 100.0)	95.3 (90.8, 99.8)
12 months	100.0 (100.0, 100.0)	95.3 (90.8, 99.8)
18 months	NE (NE, NE)	95.3 (90.8, 99.8)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	26 (21.5)	95 (40.1)
Number of Subjects Censored, n (%)	95 (78.5)	142 (59.9)
Time to first TEAE (months)		
25% percentile (95% CI)	10.18 (0.95, NE)	1.45 (0.89, 1.91)
Median (95% CI)	10.18 (NE, NE)	9.43 (5.68, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.0, 10.2	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.743 (0.223)
95% CI		(1.126, 2.698)
Log-rank p-value		0.011

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.8 (72.6, 87.1)	62.3 (56.0, 68.7)
6 months	76.9 (67.9, 85.9)	56.4 (49.1, 63.8)
9 months	76.9 (67.9, 85.9)	53.3 (45.0, 61.5)
12 months	0.0 (NE, NE)	49.7 (39.5, 59.9)
18 months	0.0 (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.63	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	16 (13.2)	62 (26.2)
Number of Subjects Censored, n (%)	105 (86.8)	175 (73.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	2.92 (1.91, 9.43)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.815 (0.282)
95% CI		(1.044, 3.158)
Log-rank p-value		0.034

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.2 (79.9, 92.5)	74.4 (68.5, 80.2)
6 months	86.2 (79.9, 92.5)	72.6 (66.4, 78.8)
9 months	86.2 (79.9, 92.5)	69.7 (62.5, 76.8)
12 months	86.2 (79.9, 92.5)	66.2 (56.7, 75.7)
18 months	NE (NE, NE)	66.2 (56.7, 75.7)
Median Follow-up Time (months)	2.79	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	2 (1.7)	12 (5.1)
Number of Subjects Censored, n (%)	119 (98.3)	225 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.391 (0.771)
95% CI		(0.528, 10.826)
Log-rank p-value		0.246

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (96.1, 100.0)	94.5 (91.3, 97.7)
6 months	98.3 (96.1, 100.0)	94.5 (91.3, 97.7)
9 months	98.3 (96.1, 100.0)	92.5 (87.5, 97.5)
12 months	98.3 (96.1, 100.0)	92.5 (87.5, 97.5)
18 months	NE (NE, NE)	92.5 (87.5, 97.5)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	2 (1.7)	6 (2.5)
Number of Subjects Censored, n (%)	119 (98.3)	231 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.159 (0.833)
95% CI		(0.226, 5.933)
Log-rank p-value		0.859

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.5, 100.0)	97.8 (95.8, 99.7)
6 months	96.3 (90.4, 100.0)	96.4 (93.2, 99.6)
9 months	96.3 (90.4, 100.0)	96.4 (93.2, 99.6)
12 months	96.3 (90.4, 100.0)	96.4 (93.2, 99.6)
18 months	NE (NE, NE)	96.4 (93.2, 99.6)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	0	9 (3.8)
Number of Subjects Censored, n (%)	121 (100.0)	228 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.047

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.9 (94.7, 99.2)
6 months	100.0 (100.0, 100.0)	96.1 (93.4, 98.8)
9 months	100.0 (100.0, 100.0)	93.4 (87.5, 99.3)
12 months	100.0 (100.0, 100.0)	93.4 (87.5, 99.3)
18 months	NE (NE, NE)	93.4 (87.5, 99.3)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	2 (1.7)	9 (3.8)
Number of Subjects Censored, n (%)	119 (98.3)	228 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.245 (0.783)
95% CI		(0.484, 10.408)
Log-rank p-value		0.299

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (96.0, 100.0)	95.9 (93.3, 98.5)
6 months	98.3 (96.0, 100.0)	95.9 (93.3, 98.5)
9 months	98.3 (96.0, 100.0)	95.9 (93.3, 98.5)
12 months	98.3 (96.0, 100.0)	95.9 (93.3, 98.5)
18 months	NE (NE, NE)	95.9 (93.3, 98.5)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	0	10 (4.2)
Number of Subjects Censored, n (%)	121 (100.0)	227 (95.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.6, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.066

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.4 (95.4, 99.5)
6 months	100.0 (100.0, 100.0)	94.3 (90.3, 98.4)
9 months	100.0 (100.0, 100.0)	92.6 (87.3, 97.8)
12 months	100.0 (100.0, 100.0)	92.6 (87.3, 97.8)
18 months	NE (NE, NE)	92.6 (87.3, 97.8)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	0	6 (2.5)
Number of Subjects Censored, n (%)	121 (100.0)	231 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.102

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.2 (95.1, 99.4)
6 months	100.0 (100.0, 100.0)	97.2 (95.1, 99.4)
9 months	100.0 (100.0, 100.0)	97.2 (95.1, 99.4)
12 months	100.0 (100.0, 100.0)	97.2 (95.1, 99.4)
18 months	NE (NE, NE)	97.2 (95.1, 99.4)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	0	8 (3.4)
Number of Subjects Censored, n (%)	121 (100.0)	229 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.063

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.9 (94.6, 99.2)
6 months	100.0 (100.0, 100.0)	96.9 (94.6, 99.2)
9 months	100.0 (100.0, 100.0)	94.2 (88.5, 99.8)
12 months	100.0 (100.0, 100.0)	94.2 (88.5, 99.8)
18 months	NE (NE, NE)	94.2 (88.5, 99.8)
Median Follow-up Time (months)	2.83	3.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	2 (1.7)	3 (1.3)
Number of Subjects Censored, n (%)	119 (98.3)	234 (98.7)
Time to first TEAE (months)		
25% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Median (95% CI)	10.18 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	10.18 (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 10.2	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.589 (0.953)
95% CI		(0.091, 3.812)
Log-rank p-value		0.585

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.5, 100.0)	98.7 (97.3, 100.0)
6 months	99.2 (97.5, 100.0)	98.7 (97.3, 100.0)
9 months	99.2 (97.5, 100.0)	98.7 (97.3, 100.0)
12 months	0.0 (NE, NE)	98.7 (97.3, 100.0)
18 months	0.0 (NE, NE)	98.7 (97.3, 100.0)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	1 (0.8)	6 (2.5)
Number of Subjects Censored, n (%)	120 (99.2)	231 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.507 (1.105)
95% CI		(0.173, 13.157)
Log-rank p-value		0.692

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.3, 100.0)	98.4 (96.6, 100.0)
6 months	99.1 (97.3, 100.0)	95.2 (91.2, 99.2)
9 months	99.1 (97.3, 100.0)	95.2 (91.2, 99.2)
12 months	99.1 (97.3, 100.0)	95.2 (91.2, 99.2)
18 months	NE (NE, NE)	95.2 (91.2, 99.2)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	31 (25.6)	97 (40.9)
Number of Subjects Censored, n (%)	90 (74.4)	140 (59.1)
Time to first TEAE (months)		
25% percentile (95% CI)	3.55 (0.99, NE)	1.61 (0.95, 2.23)
Median (95% CI)	NE (5.59, NE)	7.16 (5.78, NE)
75% percentile (95% CI)	NE (NE, NE)	16.79 (16.79, NE)
Min, Max	0.0, 6.8*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.369 (0.210)
95% CI		(0.907, 2.067)
Log-rank p-value		0.128

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.9 (68.1, 83.8)	63.6 (57.3, 69.9)
6 months	58.9 (38.4, 79.4)	56.4 (48.8, 64.0)
9 months	NE (NE, NE)	47.6 (38.4, 56.8)
12 months	NE (NE, NE)	47.6 (38.4, 56.8)
18 months	NE (NE, NE)	23.8 (0.0, 57.1)
Median Follow-up Time (months)	2.79	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	11 (9.1)	28 (11.8)
Number of Subjects Censored, n (%)	110 (90.9)	209 (88.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (7.85, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.006 (0.364)
95% CI		(0.493, 2.054)
Log-rank p-value		0.977

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.5 (84.7, 96.2)	89.7 (85.7, 93.7)
6 months	80.4 (61.1, 99.7)	86.3 (80.8, 91.7)
9 months	NE (NE, NE)	82.7 (75.5, 89.9)
12 months	NE (NE, NE)	82.7 (75.5, 89.9)
18 months	NE (NE, NE)	82.7 (75.5, 89.9)
Median Follow-up Time (months)	2.83	3.48

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	5 (4.1)	33 (13.9)
Number of Subjects Censored, n (%)	116 (95.9)	204 (86.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (6.67, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.685 (0.485)
95% CI		(1.038, 6.947)
Log-rank p-value		0.036

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.7 (93.5, 99.9)	88.4 (84.2, 92.6)
6 months	85.9 (65.9, 100.0)	83.9 (78.2, 89.5)
9 months	NE (NE, NE)	81.1 (74.5, 87.7)
12 months	NE (NE, NE)	81.1 (74.5, 87.7)
18 months	NE (NE, NE)	81.1 (74.5, 87.7)
Median Follow-up Time (months)	2.83	3.48

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	4 (3.3)	31 (13.1)
Number of Subjects Censored, n (%)	117 (96.7)	206 (86.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (6.67, NE)
Median (95% CI)	NE (5.59, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 6.8*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.150 (0.537)
95% CI		(1.100, 9.023)
Log-rank p-value		0.025

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (94.7, 100.0)	89.3 (85.2, 93.4)
6 months	86.7 (66.5, 100.0)	84.7 (79.1, 90.3)
9 months	NE (NE, NE)	81.9 (75.3, 88.5)
12 months	NE (NE, NE)	81.9 (75.3, 88.5)
18 months	NE (NE, NE)	81.9 (75.3, 88.5)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	6 (5.0)	13 (5.5)
Number of Subjects Censored, n (%)	115 (95.0)	224 (94.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.762 (0.515)
95% CI		(0.278, 2.088)
Log-rank p-value		0.570

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.0 (91.1, 98.9)	96.4 (94.0, 98.9)
6 months	95.0 (91.1, 98.9)	93.8 (90.0, 97.6)
9 months	95.0 (91.1, 98.9)	90.5 (84.7, 96.3)
12 months	95.0 (91.1, 98.9)	90.5 (84.7, 96.3)
18 months	NE (NE, NE)	90.5 (84.7, 96.3)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	1 (0.8)	14 (5.9)
Number of Subjects Censored, n (%)	120 (99.2)	223 (94.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.172 (1.040)
95% CI		(0.804, 47.398)
Log-rank p-value		0.044

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.5, 100.0)	94.6 (91.6, 97.6)
6 months	99.2 (97.5, 100.0)	94.6 (91.6, 97.6)
9 months	99.2 (97.5, 100.0)	90.4 (83.8, 97.0)
12 months	99.2 (97.5, 100.0)	90.4 (83.8, 97.0)
18 months	NE (NE, NE)	90.4 (83.8, 97.0)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	3 (2.5)	13 (5.5)
Number of Subjects Censored, n (%)	118 (97.5)	224 (94.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.755 (0.651)
95% CI		(0.490, 6.281)
Log-rank p-value		0.368

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (94.7, 100.0)	95.7 (93.1, 98.3)
6 months	97.5 (94.7, 100.0)	93.6 (89.6, 97.5)
9 months	97.5 (94.7, 100.0)	92.2 (87.5, 96.9)
12 months	97.5 (94.7, 100.0)	92.2 (87.5, 96.9)
18 months	NE (NE, NE)	92.2 (87.5, 96.9)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	2 (1.7)	12 (5.1)
Number of Subjects Censored, n (%)	119 (98.3)	225 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	7.43 (NE, NE)	NE (NE, NE)
Median (95% CI)	7.43 (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	7.43 (NE, NE)	NE (NE, NE)
Min, Max	0.0, 7.4	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.260 (0.778)
95% CI		(0.492, 10.387)
Log-rank p-value		0.274

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.6, 100.0)	94.9 (91.9, 97.9)
6 months	99.2 (97.6, 100.0)	94.0 (90.6, 97.4)
9 months	0.0 (NE, NE)	94.0 (90.6, 97.4)
12 months	0.0 (NE, NE)	94.0 (90.6, 97.4)
18 months	0.0 (NE, NE)	94.0 (90.6, 97.4)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	1 (0.8)	14 (5.9)
Number of Subjects Censored, n (%)	120 (99.2)	223 (94.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.55, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.700 (1.039)
95% CI		(0.744, 43.690)
Log-rank p-value		0.059

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.6 (91.6, 97.6)
6 months	95.8 (87.8, 100.0)	92.8 (88.9, 96.6)
9 months	95.8 (87.8, 100.0)	92.8 (88.9, 96.6)
12 months	95.8 (87.8, 100.0)	92.8 (88.9, 96.6)
18 months	NE (NE, NE)	92.8 (88.9, 96.6)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	1 (0.8)	5 (2.1)
Number of Subjects Censored, n (%)	120 (99.2)	232 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.674 (1.121)
95% CI		(0.186, 15.057)
Log-rank p-value		0.662

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.5, 100.0)	97.9 (95.8, 100.0)
6 months	99.2 (97.5, 100.0)	97.9 (95.8, 100.0)
9 months	99.2 (97.5, 100.0)	96.2 (92.4, 100.0)
12 months	99.2 (97.5, 100.0)	96.2 (92.4, 100.0)
18 months	NE (NE, NE)	96.2 (92.4, 100.0)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	1 (0.8)	4 (1.7)
Number of Subjects Censored, n (%)	120 (99.2)	233 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.331 (1.156)
95% CI		(0.138, 12.820)
Log-rank p-value		0.804

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.5, 100.0)	98.5 (96.8, 100.0)
6 months	99.2 (97.5, 100.0)	98.5 (96.8, 100.0)
9 months	99.2 (97.5, 100.0)	96.8 (93.1, 100.0)
12 months	99.2 (97.5, 100.0)	96.8 (93.1, 100.0)
18 months	NE (NE, NE)	96.8 (93.1, 100.0)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	29 (24.0)	93 (39.2)
Number of Subjects Censored, n (%)	92 (76.0)	144 (60.8)
Time to first TEAE (months)		
25% percentile (95% CI)	2.76 (1.25, NE)	0.92 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	9.69 (6.34, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.617 (0.214)
95% CI		(1.062, 2.461)
Log-rank p-value		0.025

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	74.2 (66.0, 82.5)	64.8 (58.7, 71.0)
6 months	74.2 (66.0, 82.5)	58.0 (50.5, 65.4)
9 months	74.2 (66.0, 82.5)	53.2 (44.6, 61.8)
12 months	74.2 (66.0, 82.5)	49.4 (38.7, 60.2)
18 months	NE (NE, NE)	49.4 (38.7, 60.2)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	7 (5.8)	44 (18.6)
Number of Subjects Censored, n (%)	114 (94.2)	193 (81.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.439 (0.407)
95% CI		(1.549, 7.635)
Log-rank p-value		0.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.8 (89.2, 98.3)	81.2 (76.1, 86.2)
6 months	93.8 (89.2, 98.3)	81.2 (76.1, 86.2)
9 months	93.8 (89.2, 98.3)	81.2 (76.1, 86.2)
12 months	93.8 (89.2, 98.3)	81.2 (76.1, 86.2)
18 months	NE (NE, NE)	81.2 (76.1, 86.2)
Median Follow-up Time (months)	2.83	3.09

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	11 (9.1)	25 (10.5)
Number of Subjects Censored, n (%)	110 (90.9)	212 (89.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (10.28, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.945 (0.367)
95% CI		(0.460, 1.941)
Log-rank p-value		0.846

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.5 (85.1, 95.9)	91.1 (87.3, 94.8)
6 months	90.5 (85.1, 95.9)	88.4 (83.6, 93.2)
9 months	90.5 (85.1, 95.9)	87.1 (81.7, 92.5)
12 months	90.5 (85.1, 95.9)	80.9 (68.1, 93.6)
18 months	NE (NE, NE)	80.9 (68.1, 93.6)
Median Follow-up Time (months)	2.83	3.52

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	7 (5.8)	18 (7.6)
Number of Subjects Censored, n (%)	114 (94.2)	219 (92.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.153 (0.451)
95% CI		(0.476, 2.789)
Log-rank p-value		0.738

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.0 (89.7, 98.3)	92.9 (89.5, 96.3)
6 months	94.0 (89.7, 98.3)	91.9 (87.9, 95.8)
9 months	94.0 (89.7, 98.3)	90.4 (85.7, 95.2)
12 months	94.0 (89.7, 98.3)	90.4 (85.7, 95.2)
18 months	NE (NE, NE)	90.4 (85.7, 95.2)
Median Follow-up Time (months)	2.83	3.48

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	2 (1.7)	6 (2.5)
Number of Subjects Censored, n (%)	119 (98.3)	231 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.5, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.442 (0.817)
95% CI		(0.291, 7.151)
Log-rank p-value		0.653

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (96.1, 100.0)	97.3 (95.2, 99.4)
6 months	98.3 (96.1, 100.0)	97.3 (95.2, 99.4)
9 months	98.3 (96.1, 100.0)	97.3 (95.2, 99.4)
12 months	98.3 (96.1, 100.0)	97.3 (95.2, 99.4)
18 months	NE (NE, NE)	97.3 (95.2, 99.4)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	2 (1.7)	7 (3.0)
Number of Subjects Censored, n (%)	119 (98.3)	230 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.2, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.312 (0.820)
95% CI		(0.263, 6.545)
Log-rank p-value		0.768

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (95.7, 100.0)	97.9 (96.0, 99.7)
6 months	98.2 (95.7, 100.0)	96.7 (93.7, 99.6)
9 months	98.2 (95.7, 100.0)	95.3 (91.2, 99.3)
12 months	98.2 (95.7, 100.0)	95.3 (91.2, 99.3)
18 months	NE (NE, NE)	95.3 (91.2, 99.3)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Vascular disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	16 (13.2)	89 (37.6)
Number of Subjects Censored, n (%)	105 (86.8)	148 (62.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.89 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	NE (7.39, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.955 (0.273)
95% CI		(1.730, 5.048)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Vascular disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.9 (79.5, 92.4)	64.1 (57.9, 70.4)
6 months	85.9 (79.5, 92.4)	62.3 (55.7, 68.8)
9 months	NE (NE, NE)	54.9 (45.9, 63.9)
12 months	NE (NE, NE)	54.9 (45.9, 63.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	12 (9.9)	87 (36.7)
Number of Subjects Censored, n (%)	109 (90.1)	150 (63.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.95 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	NE (7.13, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.829 (0.310)
95% CI		(2.087, 7.023)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.4 (83.7, 95.2)	65.4 (59.2, 71.6)
6 months	89.4 (83.7, 95.2)	63.5 (57.0, 70.0)
9 months	NE (NE, NE)	54.2 (44.8, 63.6)
12 months	NE (NE, NE)	54.2 (44.8, 63.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	32 (26.4)	71 (30.0)
Number of Subjects Censored, n (%)	89 (73.6)	166 (70.0)
Time to first TEAE (months)		
25% percentile (95% CI)	2.83 (1.25, 5.59)	2.04 (0.99, 5.29)
Median (95% CI)	5.59 (5.59, NE)	NE (8.64, NE)
75% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.985 (0.217)
95% CI		(0.644, 1.506)
Log-rank p-value		0.957

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	74.0 (65.6, 82.4)	72.6 (66.7, 78.4)
6 months	49.0 (19.5, 78.5)	66.5 (59.1, 74.0)
9 months	NE (NE, NE)	59.2 (48.7, 69.8)
12 months	NE (NE, NE)	59.2 (48.7, 69.8)
18 months	NE (NE, NE)	59.2 (48.7, 69.8)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	10 (8.3)	21 (8.9)
Number of Subjects Censored, n (%)	111 (91.7)	216 (91.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.926 (0.388)
95% CI		(0.433, 1.981)
Log-rank p-value		0.823

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.6 (86.5, 96.6)	91.9 (88.3, 95.5)
6 months	91.6 (86.5, 96.6)	89.2 (84.5, 93.9)
9 months	91.6 (86.5, 96.6)	89.2 (84.5, 93.9)
12 months	91.6 (86.5, 96.6)	89.2 (84.5, 93.9)
18 months	NE (NE, NE)	89.2 (84.5, 93.9)
Median Follow-up Time (months)	2.83	3.48

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	8 (6.6)	23 (9.7)
Number of Subjects Censored, n (%)	113 (93.4)	214 (90.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.59, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.200 (0.417)
95% CI		(0.529, 2.718)
Log-rank p-value		0.691

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.9 (89.6, 98.3)	91.6 (88.0, 95.3)
6 months	83.5 (63.8, 100.0)	88.6 (83.6, 93.6)
9 months	NE (NE, NE)	86.9 (80.9, 92.8)
12 months	NE (NE, NE)	86.9 (80.9, 92.8)
18 months	NE (NE, NE)	86.9 (80.9, 92.8)
Median Follow-up Time (months)	2.83	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	4 (3.3)	9 (3.8)
Number of Subjects Censored, n (%)	117 (96.7)	228 (96.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.004 (0.607)
95% CI		(0.306, 3.297)
Log-rank p-value		0.945

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (95.6, 100.0)	96.1 (93.6, 98.6)
6 months	89.6 (78.1, 100.0)	96.1 (93.6, 98.6)
9 months	89.6 (78.1, 100.0)	96.1 (93.6, 98.6)
12 months	89.6 (78.1, 100.0)	96.1 (93.6, 98.6)
18 months	NE (NE, NE)	96.1 (93.6, 98.6)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	2 (1.7)	5 (2.1)
Number of Subjects Censored, n (%)	119 (98.3)	232 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.935 (0.860)
95% CI		(0.173, 5.040)
Log-rank p-value		0.888

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (95.9, 100.0)	98.2 (96.4, 100.0)
6 months	98.3 (95.9, 100.0)	96.8 (93.6, 100.0)
9 months	98.3 (95.9, 100.0)	96.8 (93.6, 100.0)
12 months	98.3 (95.9, 100.0)	96.8 (93.6, 100.0)
18 months	NE (NE, NE)	96.8 (93.6, 100.0)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	2 (1.7)	10 (4.2)
Number of Subjects Censored, n (%)	119 (98.3)	227 (95.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.820 (0.792)
95% CI		(0.385, 8.597)
Log-rank p-value		0.441

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (96.0, 100.0)	97.0 (94.7, 99.2)
6 months	98.3 (96.0, 100.0)	95.7 (92.3, 99.0)
9 months	98.3 (96.0, 100.0)	91.1 (84.0, 98.3)
12 months	98.3 (96.0, 100.0)	91.1 (84.0, 98.3)
18 months	NE (NE, NE)	91.1 (84.0, 98.3)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	0	6 (2.5)
Number of Subjects Censored, n (%)	121 (100.0)	231 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.107

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.3 (95.2, 99.4)
6 months	100.0 (100.0, 100.0)	97.3 (95.2, 99.4)
9 months	100.0 (100.0, 100.0)	97.3 (95.2, 99.4)
12 months	100.0 (100.0, 100.0)	97.3 (95.2, 99.4)
18 months	NE (NE, NE)	97.3 (95.2, 99.4)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	13 (10.7)	65 (27.4)
Number of Subjects Censored, n (%)	108 (89.3)	172 (72.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	2.33 (1.28, NE)
Median (95% CI)	NE (NE, NE)	13.14 (13.14, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.14, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.538 (0.306)
95% CI		(1.395, 4.620)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.8 (84.4, 95.3)	74.2 (68.5, 79.8)
6 months	85.3 (75.3, 95.4)	71.3 (65.0, 77.7)
9 months	85.3 (75.3, 95.4)	69.5 (62.4, 76.6)
12 months	85.3 (75.3, 95.4)	69.5 (62.4, 76.6)
18 months	NE (NE, NE)	46.3 (9.0, 83.7)
Median Follow-up Time (months)	2.79	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	0	27 (11.4)
Number of Subjects Censored, n (%)	121 (100.0)	210 (88.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	90.5 (86.7, 94.3)
6 months	100.0 (100.0, 100.0)	86.6 (81.3, 91.9)
9 months	100.0 (100.0, 100.0)	84.7 (78.4, 91.0)
12 months	100.0 (100.0, 100.0)	84.7 (78.4, 91.0)
18 months	NE (NE, NE)	84.7 (78.4, 91.0)
Median Follow-up Time (months)	2.83	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	4 (3.3)	8 (3.4)
Number of Subjects Censored, n (%)	117 (96.7)	229 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.990 (0.613)
95% CI		(0.298, 3.294)
Log-rank p-value		0.999

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.7 (93.5, 99.9)	96.6 (94.3, 98.9)
6 months	96.7 (93.5, 99.9)	96.6 (94.3, 98.9)
9 months	96.7 (93.5, 99.9)	96.6 (94.3, 98.9)
12 months	96.7 (93.5, 99.9)	96.6 (94.3, 98.9)
18 months	NE (NE, NE)	96.6 (94.3, 98.9)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	2 (1.7)	6 (2.5)
Number of Subjects Censored, n (%)	119 (98.3)	231 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.431 (0.822)
95% CI		(0.286, 7.168)
Log-rank p-value		0.697

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.5, 100.0)	97.4 (95.4, 99.5)
6 months	95.0 (87.0, 100.0)	97.4 (95.4, 99.5)
9 months	95.0 (87.0, 100.0)	97.4 (95.4, 99.5)
12 months	95.0 (87.0, 100.0)	97.4 (95.4, 99.5)
18 months	NE (NE, NE)	97.4 (95.4, 99.5)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	21 (17.4)	58 (24.5)
Number of Subjects Censored, n (%)	100 (82.6)	179 (75.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.87, NE)	4.01 (2.27, NE)
Median (95% CI)	NE (NE, NE)	NE (11.10, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.235 (0.257)
95% CI		(0.746, 2.044)
Log-rank p-value		0.430

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.7 (74.5, 88.8)	78.8 (73.5, 84.1)
6 months	81.7 (74.5, 88.8)	72.3 (65.5, 79.1)
9 months	81.7 (74.5, 88.8)	71.0 (63.8, 78.1)
12 months	81.7 (74.5, 88.8)	64.5 (50.8, 78.2)
18 months	NE (NE, NE)	64.5 (50.8, 78.2)
Median Follow-up Time (months)	2.60	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	7 (5.8)	18 (7.6)
Number of Subjects Censored, n (%)	114 (94.2)	219 (92.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.257 (0.448)
95% CI		(0.522, 3.026)
Log-rank p-value		0.622

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.0 (89.7, 98.3)	92.7 (89.4, 96.1)
6 months	94.0 (89.7, 98.3)	92.7 (89.4, 96.1)
9 months	94.0 (89.7, 98.3)	91.3 (87.1, 95.6)
12 months	94.0 (89.7, 98.3)	91.3 (87.1, 95.6)
18 months	NE (NE, NE)	91.3 (87.1, 95.6)
Median Follow-up Time (months)	2.83	3.48

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	4 (3.3)	4 (1.7)
Number of Subjects Censored, n (%)	117 (96.7)	233 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.484 (0.708)
95% CI		(0.121, 1.939)
Log-rank p-value		0.298

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.7 (93.5, 99.9)	98.3 (96.6, 100.0)
6 months	96.7 (93.5, 99.9)	98.3 (96.6, 100.0)
9 months	96.7 (93.5, 99.9)	98.3 (96.6, 100.0)
12 months	96.7 (93.5, 99.9)	98.3 (96.6, 100.0)
18 months	NE (NE, NE)	98.3 (96.6, 100.0)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	4 (3.3)	5 (2.1)
Number of Subjects Censored, n (%)	117 (96.7)	232 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.621 (0.671)
95% CI		(0.166, 2.315)
Log-rank p-value		0.505

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.5 (93.1, 99.9)	97.8 (95.9, 99.7)
6 months	96.5 (93.1, 99.9)	97.8 (95.9, 99.7)
9 months	96.5 (93.1, 99.9)	97.8 (95.9, 99.7)
12 months	96.5 (93.1, 99.9)	97.8 (95.9, 99.7)
18 months	NE (NE, NE)	97.8 (95.9, 99.7)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	12 (9.9)	58 (24.5)
Number of Subjects Censored, n (%)	109 (90.1)	179 (75.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.57 (2.76, 13.60)
Median (95% CI)	NE (NE, NE)	13.60 (13.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.015 (0.321)
95% CI		(1.075, 3.778)
Log-rank p-value		0.028

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.3 (83.5, 95.0)	79.1 (73.8, 84.5)
6 months	89.3 (83.5, 95.0)	71.8 (64.9, 78.7)
9 months	89.3 (83.5, 95.0)	68.7 (60.9, 76.6)
12 months	89.3 (83.5, 95.0)	68.7 (60.9, 76.6)
18 months	NE (NE, NE)	34.4 (0.0, 82.2)
Median Follow-up Time (months)	2.79	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	3 (2.5)	38 (16.0)
Number of Subjects Censored, n (%)	118 (97.5)	199 (84.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.60 (6.93, NE)
Median (95% CI)	NE (NE, NE)	13.60 (13.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (13.60, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.335 (0.603)
95% CI		(1.637, 17.388)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (94.4, 100.0)	86.0 (81.4, 90.6)
6 months	97.3 (94.4, 100.0)	81.8 (76.2, 87.5)
9 months	97.3 (94.4, 100.0)	80.1 (73.5, 86.6)
12 months	97.3 (94.4, 100.0)	80.1 (73.5, 86.6)
18 months	NE (NE, NE)	40.0 (0.0, 95.6)
Median Follow-up Time (months)	2.83	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	2 (1.7)	7 (3.0)
Number of Subjects Censored, n (%)	119 (98.3)	230 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.626 (0.803)
95% CI		(0.337, 7.846)
Log-rank p-value		0.553

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.2 (95.7, 100.0)	97.0 (94.8, 99.2)
6 months	98.2 (95.7, 100.0)	97.0 (94.8, 99.2)
9 months	98.2 (95.7, 100.0)	97.0 (94.8, 99.2)
12 months	98.2 (95.7, 100.0)	97.0 (94.8, 99.2)
18 months	NE (NE, NE)	97.0 (94.8, 99.2)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	18 (14.9)	56 (23.6)
Number of Subjects Censored, n (%)	103 (85.1)	181 (76.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.15, NE)	5.52 (3.52, 6.87)
Median (95% CI)	NE (NE, NE)	17.48 (7.92, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.48, NE)
Min, Max	0.0, 13.0*	0.1, 19.8*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.056 (0.281)
95% CI		(0.609, 1.830)
Log-rank p-value		0.780

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.9 (79.4, 92.4)	83.2 (78.2, 88.2)
6 months	79.1 (68.0, 90.1)	72.6 (65.2, 80.1)
9 months	79.1 (68.0, 90.1)	60.3 (49.8, 70.7)
12 months	79.1 (68.0, 90.1)	60.3 (49.8, 70.7)
18 months	NE (NE, NE)	30.1 (0.0, 72.2)
Median Follow-up Time (months)	2.83	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	7 (5.8)	10 (4.2)
Number of Subjects Censored, n (%)	114 (94.2)	227 (95.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.399 (0.528)
95% CI		(0.142, 1.122)
Log-rank p-value		0.098

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.7 (93.5, 99.9)	97.4 (95.4, 99.5)
6 months	82.9 (67.1, 98.8)	95.2 (91.5, 98.9)
9 months	82.9 (67.1, 98.8)	92.1 (86.6, 97.6)
12 months	82.9 (67.1, 98.8)	92.1 (86.6, 97.6)
18 months	NE (NE, NE)	92.1 (86.6, 97.6)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	3 (2.5)	7 (3.0)
Number of Subjects Censored, n (%)	118 (97.5)	230 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.611 (0.722)
95% CI		(0.149, 2.517)
Log-rank p-value		0.427

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (94.0, 100.0)	99.1 (97.8, 100.0)
6 months	97.2 (94.0, 100.0)	95.5 (91.9, 99.2)
9 months	97.2 (94.0, 100.0)	94.0 (89.3, 98.7)
12 months	97.2 (94.0, 100.0)	94.0 (89.3, 98.7)
18 months	NE (NE, NE)	94.0 (89.3, 98.7)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	0	3 (1.3)
Number of Subjects Censored, n (%)	121 (100.0)	234 (98.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.1, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.392

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.9 (97.4, 100.0)
6 months	100.0 (100.0, 100.0)	97.6 (94.7, 100.0)
9 months	100.0 (100.0, 100.0)	97.6 (94.7, 100.0)
12 months	100.0 (100.0, 100.0)	97.6 (94.7, 100.0)
18 months	NE (NE, NE)	97.6 (94.7, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	22 (18.2)	37 (15.6)
Number of Subjects Censored, n (%)	99 (81.8)	200 (84.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.04, NE)	NE (6.47, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.749 (0.273)
95% CI		(0.438, 1.280)
Log-rank p-value		0.292

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.0 (72.4, 87.6)	86.0 (81.5, 90.5)
6 months	80.0 (72.4, 87.6)	83.2 (77.8, 88.7)
9 months	80.0 (72.4, 87.6)	80.2 (73.5, 86.9)
12 months	80.0 (72.4, 87.6)	80.2 (73.5, 86.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	17 (14.0)	20 (8.4)
Number of Subjects Censored, n (%)	104 (86.0)	217 (91.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	17.74 (17.74, NE)
Median (95% CI)	NE (NE, NE)	17.74 (17.74, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (17.74, NE)
Min, Max	0.2*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.430 (0.343)
95% CI		(0.219, 0.842)
Log-rank p-value		0.013

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.2 (77.2, 91.2)	93.6 (90.4, 96.9)
6 months	84.2 (77.2, 91.2)	89.7 (84.6, 94.7)
9 months	84.2 (77.2, 91.2)	88.3 (82.7, 93.9)
12 months	84.2 (77.2, 91.2)	88.3 (82.7, 93.9)
18 months	NE (NE, NE)	44.2 (0.0, 100.0)
Median Follow-up Time (months)	2.76	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	2 (1.7)	20 (8.4)
Number of Subjects Censored, n (%)	119 (98.3)	217 (91.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.121 (0.742)
95% CI		(1.196, 21.923)
Log-rank p-value		0.014

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (96.0, 100.0)	91.5 (87.9, 95.1)
6 months	98.3 (96.0, 100.0)	91.5 (87.9, 95.1)
9 months	98.3 (96.0, 100.0)	91.5 (87.9, 95.1)
12 months	98.3 (96.0, 100.0)	91.5 (87.9, 95.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.48

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Endocrine disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	1 (0.8)	49 (20.7)
Number of Subjects Censored, n (%)	120 (99.2)	188 (79.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.75 (3.48, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		20.254 (1.012)
95% CI		(2.789, 147.091)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Endocrine disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.5, 100.0)	82.7 (77.6, 87.7)
6 months	99.2 (97.5, 100.0)	72.4 (64.6, 80.3)
9 months	99.2 (97.5, 100.0)	70.9 (62.7, 79.2)
12 months	99.2 (97.5, 100.0)	66.8 (55.7, 77.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	1 (0.8)	45 (19.0)
Number of Subjects Censored, n (%)	120 (99.2)	192 (81.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.98 (3.84, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		18.067 (1.013)
95% CI		(2.482, 131.510)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.5, 100.0)	84.4 (79.5, 89.2)
6 months	99.2 (97.5, 100.0)	74.1 (66.3, 81.9)
9 months	99.2 (97.5, 100.0)	72.6 (64.4, 80.8)
12 months	99.2 (97.5, 100.0)	68.6 (57.7, 79.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.09

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	11 (9.1)	30 (12.7)
Number of Subjects Censored, n (%)	110 (90.9)	207 (87.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.064 (0.357)
95% CI		(0.528, 2.142)
Log-rank p-value		0.882

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	91.5 (86.5, 96.6)	89.4 (85.2, 93.5)
6 months	88.9 (81.9, 95.9)	84.2 (78.6, 89.9)
9 months	88.9 (81.9, 95.9)	82.8 (76.5, 89.0)
12 months	88.9 (81.9, 95.9)	82.8 (76.5, 89.0)
18 months	NE (NE, NE)	82.8 (76.5, 89.0)
Median Follow-up Time (months)	2.83	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	7 (5.8)	13 (5.5)
Number of Subjects Censored, n (%)	114 (94.2)	224 (94.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.618 (0.477)
95% CI		(0.243, 1.575)
Log-rank p-value		0.261

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.0 (89.7, 98.3)	95.9 (93.0, 98.7)
6 months	94.0 (89.7, 98.3)	92.3 (87.9, 96.8)
9 months	94.0 (89.7, 98.3)	90.8 (85.5, 96.1)
12 months	94.0 (89.7, 98.3)	90.8 (85.5, 96.1)
18 months	NE (NE, NE)	90.8 (85.5, 96.1)
Median Follow-up Time (months)	2.83	3.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	2 (1.7)	6 (2.5)
Number of Subjects Censored, n (%)	119 (98.3)	231 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.0, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.250 (0.822)
95% CI		(0.250, 6.265)
Log-rank p-value		0.799

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.1 (97.3, 100.0)	97.2 (94.9, 99.4)
6 months	96.3 (90.7, 100.0)	97.2 (94.9, 99.4)
9 months	96.3 (90.7, 100.0)	97.2 (94.9, 99.4)
12 months	96.3 (90.7, 100.0)	97.2 (94.9, 99.4)
18 months	NE (NE, NE)	97.2 (94.9, 99.4)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	1 (0.8)	6 (2.5)
Number of Subjects Censored, n (%)	120 (99.2)	231 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.3, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.779 (1.085)
95% CI		(0.331, 23.319)
Log-rank p-value		0.341

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.5, 100.0)	97.8 (96.0, 99.7)
6 months	99.2 (97.5, 100.0)	97.0 (94.6, 99.5)
9 months	99.2 (97.5, 100.0)	97.0 (94.6, 99.5)
12 months	99.2 (97.5, 100.0)	97.0 (94.6, 99.5)
18 months	NE (NE, NE)	97.0 (94.6, 99.5)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	10 (8.3)	24 (10.1)
Number of Subjects Censored, n (%)	111 (91.7)	213 (89.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 13.0*	0.4, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.939 (0.383)
95% CI		(0.443, 1.989)
Log-rank p-value		0.922

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.5 (87.8, 97.2)	91.2 (87.3, 95.0)
6 months	89.9 (83.2, 96.7)	87.5 (82.3, 92.7)
9 months	89.9 (83.2, 96.7)	85.6 (79.4, 91.8)
12 months	89.9 (83.2, 96.7)	85.6 (79.4, 91.8)
18 months	NE (NE, NE)	85.6 (79.4, 91.8)
Median Follow-up Time (months)	2.83	3.48

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	1 (0.8)	7 (3.0)
Number of Subjects Censored, n (%)	120 (99.2)	230 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.8*, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.695 (1.076)
95% CI		(0.327, 22.219)
Log-rank p-value		0.349

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.5, 100.0)	97.0 (94.5, 99.4)
6 months	99.2 (97.5, 100.0)	96.1 (93.1, 99.0)
9 months	99.2 (97.5, 100.0)	96.1 (93.1, 99.0)
12 months	99.2 (97.5, 100.0)	96.1 (93.1, 99.0)
18 months	NE (NE, NE)	96.1 (93.1, 99.0)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Number of Subjects with Events, n (%)	0	5 (2.1)
Number of Subjects Censored, n (%)	121 (100.0)	232 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2*, 13.0*	0.7, 20.1*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.167

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
TAS-102

Statistics	Placebo + BSC N=121	Fruquintinib + BSC N=237
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.3 (96.7, 100.0)
6 months	100.0 (100.0, 100.0)	98.3 (96.7, 100.0)
9 months	100.0 (100.0, 100.0)	96.4 (92.3, 100.0)
12 months	100.0 (100.0, 100.0)	96.4 (92.3, 100.0)
18 months	NE (NE, NE)	96.4 (92.3, 100.0)
Median Follow-up Time (months)	2.83	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	8 (44.4)	25 (62.5)
Number of Subjects Censored, n (%)	10 (55.6)	15 (37.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.92 (0.46, 2.76)	0.48 (0.23, 1.05)
Median (95% CI)	NE (0.92, NE)	2.79 (0.69, 4.96)
75% percentile (95% CI)	NE (NE, NE)	NE (4.70, NE)
Min, Max	0.5, 6.5*	0.0, 10.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.753 (0.432)
95% CI		(0.751, 4.091)
Log-rank p-value		0.197

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	53.0 (28.7, 77.3)	50.0 (34.5, 65.5)
6 months	53.0 (28.7, 77.3)	34.3 (18.6, 50.0)
9 months	NE (NE, NE)	34.3 (18.6, 50.0)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.69

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	4 (22.2)	12 (30.0)
Number of Subjects Censored, n (%)	14 (77.8)	28 (70.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.46, NE)	3.15 (0.69, NE)
Median (95% CI)	NE (NE, NE)	NE (3.25, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.5, 6.5*	0.1, 10.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.660 (0.647)
95% CI		(0.467, 5.901)
Log-rank p-value		0.438

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.8 (58.6, 97.0)	79.8 (67.2, 92.3)
6 months	77.8 (58.6, 97.0)	64.1 (46.9, 81.3)
9 months	NE (NE, NE)	64.1 (46.9, 81.3)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.19

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	3 (16.7)	9 (22.5)
Number of Subjects Censored, n (%)	15 (83.3)	31 (77.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	NE (0.46, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 6.5*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.579 (0.673)
95% CI		(0.422, 5.912)
Log-rank p-value		0.537

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.0 (65.4, 100.0)	76.4 (62.8, 90.0)
6 months	83.0 (65.4, 100.0)	76.4 (62.8, 90.0)
9 months	NE (NE, NE)	76.4 (62.8, 90.0)
12 months	NE (NE, NE)	76.4 (62.8, 90.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.74	3.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	5 (27.8)	4 (10.0)
Number of Subjects Censored, n (%)	13 (72.2)	36 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	2.76 (0.46, NE)	11.53 (11.53, NE)
Median (95% CI)	NE (2.76, NE)	NE (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Min, Max	0.5, 6.5*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.273 (0.736)
95% CI		(0.065, 1.154)
Log-rank p-value		0.057

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	67.7 (43.1, 92.3)	92.5 (84.3, 100.0)
6 months	67.7 (43.1, 92.3)	92.5 (84.3, 100.0)
9 months	NE (NE, NE)	92.5 (84.3, 100.0)
12 months	NE (NE, NE)	61.7 (12.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	3 (7.5)
Number of Subjects Censored, n (%)	18 (100.0)	37 (92.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	13.24 (NE, NE)
Median (95% CI)	NE (NE, NE)	13.24 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	13.24 (NE, NE)
Min, Max	1.8*, 6.5*	0.7, 13.2
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.371

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.5 (92.7, 100.0)
6 months	100.0 (100.0, 100.0)	93.6 (84.8, 100.0)
9 months	NE (NE, NE)	93.6 (84.8, 100.0)
12 months	NE (NE, NE)	93.6 (84.8, 100.0)
18 months	NE (NE, NE)	0.0 (NE, NE)
Median Follow-up Time (months)	2.83	4.16

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	4 (10.0)
Number of Subjects Censored, n (%)	18 (100.0)	36 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.22, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	1.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.231

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	92.3 (83.9, 100.0)
6 months	100.0 (100.0, 100.0)	88.7 (78.2, 99.3)
9 months	NE (NE, NE)	88.7 (78.2, 99.3)
12 months	NE (NE, NE)	88.7 (78.2, 99.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	2 (11.1)	4 (10.0)
Number of Subjects Censored, n (%)	16 (88.9)	36 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	9.99 (9.99, NE)
Median (95% CI)	NE (NE, NE)	NE (9.99, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (9.99, NE)
Min, Max	0.7, 6.5*	0.7, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.570 (0.918)
95% CI		(0.094, 3.445)
Log-rank p-value		0.529

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (74.4, 100.0)	92.3 (83.9, 100.0)
6 months	88.9 (74.4, 100.0)	92.3 (83.9, 100.0)
9 months	NE (NE, NE)	92.3 (83.9, 100.0)
12 months	NE (NE, NE)	69.2 (29.5, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	1 (2.5)
Number of Subjects Censored, n (%)	17 (94.4)	39 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.91, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	1.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.464 (1.426)
95% CI		(0.028, 7.584)
Log-rank p-value		0.546

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.1 (82.9, 100.0)	97.5 (92.7, 100.0)
6 months	94.1 (82.9, 100.0)	97.5 (92.7, 100.0)
9 months	NE (NE, NE)	97.5 (92.7, 100.0)
12 months	NE (NE, NE)	97.5 (92.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	13 (72.2)	27 (67.5)
Number of Subjects Censored, n (%)	5 (27.8)	13 (32.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.66 (0.03, 0.69)	0.69 (0.46, 1.18)
Median (95% CI)	0.72 (0.66, 3.75)	2.76 (1.05, 4.63)
75% percentile (95% CI)	3.75 (0.72, NE)	4.90 (4.07, NE)
Min, Max	0.0, 5.6*	0.2, 10.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.654 (0.343)
95% CI		(0.334, 1.280)
Log-rank p-value		0.257

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	33.3 (11.6, 55.1)	48.0 (31.9, 64.1)
6 months	NE (NE, NE)	22.0 (6.0, 37.9)
9 months	NE (NE, NE)	14.7 (0.0, 30.5)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	0.72	1.59

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	5 (27.8)	6 (15.0)
Number of Subjects Censored, n (%)	13 (72.2)	34 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.77 (0.07, NE)	10.87 (2.56, NE)
Median (95% CI)	NE (1.77, NE)	10.87 (10.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (10.87, NE)
Min, Max	0.1, 6.5*	0.2, 12.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.353 (0.640)
95% CI		(0.101, 1.237)
Log-rank p-value		0.070

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.2 (51.5, 92.9)	89.3 (79.4, 99.3)
6 months	72.2 (51.5, 92.9)	85.4 (73.4, 97.5)
9 months	NE (NE, NE)	85.4 (73.4, 97.5)
12 months	NE (NE, NE)	42.7 (0.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	6 (33.3)	8 (20.0)
Number of Subjects Censored, n (%)	12 (66.7)	32 (80.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.61 (0.30, NE)	4.21 (2.89, NE)
Median (95% CI)	NE (1.61, NE)	NE (4.63, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 6.5*	1.0*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.356 (0.560)
95% CI		(0.119, 1.068)
Log-rank p-value		0.066

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	66.2 (44.1, 88.3)	86.6 (74.4, 98.9)
6 months	66.2 (44.1, 88.3)	68.8 (50.2, 87.3)
9 months	NE (NE, NE)	68.8 (50.2, 87.3)
12 months	NE (NE, NE)	68.8 (50.2, 87.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.37	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	4 (22.2)	8 (20.0)
Number of Subjects Censored, n (%)	14 (77.8)	32 (80.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.10, NE)	6.18 (3.55, NE)
Median (95% CI)	NE (NE, NE)	NE (6.18, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (7.98, NE)
Min, Max	0.1, 6.5*	0.4, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.593 (0.644)
95% CI		(0.168, 2.093)
Log-rank p-value		0.457

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.4 (57.8, 96.9)	91.7 (82.5, 100.0)
6 months	77.4 (57.8, 96.9)	78.4 (62.5, 94.4)
9 months	NE (NE, NE)	57.5 (28.1, 87.0)
12 months	NE (NE, NE)	57.5 (28.1, 87.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	2 (11.1)	4 (10.0)
Number of Subjects Censored, n (%)	16 (88.9)	36 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	NE (4.70, NE)
Median (95% CI)	NE (NE, NE)	NE (6.80, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	1.0*, 12.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.478 (0.921)
95% CI		(0.079, 2.908)
Log-rank p-value		0.466

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (74.4, 100.0)	93.4 (84.5, 100.0)
6 months	88.9 (74.4, 100.0)	88.5 (75.9, 100.0)
9 months	NE (NE, NE)	75.8 (50.5, 100.0)
12 months	NE (NE, NE)	75.8 (50.5, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	4.16

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	4 (22.2)	7 (17.5)
Number of Subjects Censored, n (%)	14 (77.8)	33 (82.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.33, NE)	NE (1.61, NE)
Median (95% CI)	NE (1.97, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 6.5*	0.8, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.683 (0.639)
95% CI		(0.195, 2.389)
Log-rank p-value		0.690

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	76.0 (55.4, 96.7)	86.0 (74.4, 97.5)
6 months	76.0 (55.4, 96.7)	76.9 (61.2, 92.7)
9 months	NE (NE, NE)	76.9 (61.2, 92.7)
12 months	NE (NE, NE)	76.9 (61.2, 92.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	7 (17.5)
Number of Subjects Censored, n (%)	18 (100.0)	33 (82.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	7.98 (1.08, NE)
Median (95% CI)	NE (NE, NE)	NE (7.98, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	0.2, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.097

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	84.5 (73.1, 95.9)
6 months	100.0 (100.0, 100.0)	84.5 (73.1, 95.9)
9 months	NE (NE, NE)	70.5 (43.5, 97.4)
12 months	NE (NE, NE)	70.5 (43.5, 97.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	5 (12.5)
Number of Subjects Censored, n (%)	18 (100.0)	35 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (1.84, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	0.4, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.163

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	89.5 (79.7, 99.3)
6 months	100.0 (100.0, 100.0)	84.8 (71.9, 97.7)
9 months	NE (NE, NE)	84.8 (71.9, 97.7)
12 months	NE (NE, NE)	84.8 (71.9, 97.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	3 (7.5)
Number of Subjects Censored, n (%)	18 (100.0)	37 (92.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.44, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	0.5, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.274

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.9 (88.1, 100.0)
6 months	100.0 (100.0, 100.0)	89.9 (78.4, 100.0)
9 months	NE (NE, NE)	89.9 (78.4, 100.0)
12 months	NE (NE, NE)	89.9 (78.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	0
Number of Subjects Censored, n (%)	17 (94.4)	40 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.94, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	1.0*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.221

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	100.0 (100.0, 100.0)
6 months	92.3 (77.8, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	2 (11.1)	0
Number of Subjects Censored, n (%)	16 (88.9)	40 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.66, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	1.0*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.034

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (74.4, 100.0)	100.0 (100.0, 100.0)
6 months	88.9 (74.4, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	2 (5.0)
Number of Subjects Censored, n (%)	18 (100.0)	38 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	0.7, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.250

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.4 (86.7, 100.0)
6 months	100.0 (100.0, 100.0)	94.4 (86.7, 100.0)
9 months	NE (NE, NE)	94.4 (86.7, 100.0)
12 months	NE (NE, NE)	94.4 (86.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	6 (33.3)	16 (40.0)
Number of Subjects Censored, n (%)	12 (66.7)	24 (60.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.03, NE)	1.58 (0.69, 3.94)
Median (95% CI)	NE (1.87, NE)	6.24 (2.86, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (6.24, NE)
Min, Max	0.0, 6.5*	0.6, 9.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.275 (0.519)
95% CI		(0.461, 3.524)
Log-rank p-value		0.612

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	64.2 (40.6, 87.8)	67.4 (52.0, 82.9)
6 months	64.2 (40.6, 87.8)	51.5 (31.5, 71.6)
9 months	NE (NE, NE)	42.9 (20.3, 65.6)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	2.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	2 (11.1)	7 (17.5)
Number of Subjects Censored, n (%)	16 (88.9)	33 (82.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (1.38, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 6.5*	0.6, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.380 (0.817)
95% CI		(0.278, 6.841)
Log-rank p-value		0.767

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.5 (73.6, 100.0)	87.0 (76.3, 97.7)
6 months	88.5 (73.6, 100.0)	82.6 (69.5, 95.7)
9 months	NE (NE, NE)	76.3 (59.2, 93.3)
12 months	NE (NE, NE)	76.3 (59.2, 93.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	1 (2.5)
Number of Subjects Censored, n (%)	17 (94.4)	39 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.03, NE)	NE (3.94, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	1.0*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.350 (1.415)
95% CI		(0.022, 5.607)
Log-rank p-value		0.438

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (83.9, 100.0)	100.0 (100.0, 100.0)
6 months	94.4 (83.9, 100.0)	95.2 (86.1, 100.0)
9 months	NE (NE, NE)	95.2 (86.1, 100.0)
12 months	NE (NE, NE)	95.2 (86.1, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	1 (2.5)
Number of Subjects Censored, n (%)	18 (100.0)	39 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.07, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	1.0*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.564

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	100.0 (100.0, 100.0)	95.2 (86.1, 100.0)
9 months	NE (NE, NE)	95.2 (86.1, 100.0)
12 months	NE (NE, NE)	95.2 (86.1, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	2 (5.0)
Number of Subjects Censored, n (%)	18 (100.0)	38 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	0.9, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.373

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.3 (86.4, 100.0)
6 months	100.0 (100.0, 100.0)	94.3 (86.4, 100.0)
9 months	NE (NE, NE)	94.3 (86.4, 100.0)
12 months	NE (NE, NE)	94.3 (86.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.16

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	1 (2.5)
Number of Subjects Censored, n (%)	18 (100.0)	39 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.16, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	1.0*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.724

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	100.0 (100.0, 100.0)	94.1 (82.9, 100.0)
9 months	NE (NE, NE)	94.1 (82.9, 100.0)
12 months	NE (NE, NE)	94.1 (82.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	1 (2.5)
Number of Subjects Censored, n (%)	18 (100.0)	39 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	0.7, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.465

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.5 (92.7, 100.0)
6 months	100.0 (100.0, 100.0)	97.5 (92.7, 100.0)
9 months	NE (NE, NE)	97.5 (92.7, 100.0)
12 months	NE (NE, NE)	97.5 (92.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.30

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	3 (16.7)	0
Number of Subjects Censored, n (%)	15 (83.3)	40 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.43, NE)	NE (NE, NE)
Median (95% CI)	NE (2.83, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4, 6.5*	1.0*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.021

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.0 (58.9, 100.0)	100.0 (100.0, 100.0)
6 months	80.0 (58.9, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	1 (2.5)
Number of Subjects Censored, n (%)	18 (100.0)	39 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	1.0*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.617

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	100.0 (100.0, 100.0)	96.2 (88.8, 100.0)
9 months	NE (NE, NE)	96.2 (88.8, 100.0)
12 months	NE (NE, NE)	96.2 (88.8, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.16

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	4 (10.0)
Number of Subjects Censored, n (%)	18 (100.0)	36 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	0.7, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.180

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	90.0 (80.7, 99.3)
6 months	100.0 (100.0, 100.0)	90.0 (80.7, 99.3)
9 months	NE (NE, NE)	90.0 (80.7, 99.3)
12 months	NE (NE, NE)	90.0 (80.7, 99.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	3 (7.5)
Number of Subjects Censored, n (%)	18 (100.0)	37 (92.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (4.21, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	0.7, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.318

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.5 (92.7, 100.0)
6 months	100.0 (100.0, 100.0)	86.8 (72.2, 100.0)
9 months	NE (NE, NE)	86.8 (72.2, 100.0)
12 months	NE (NE, NE)	86.8 (72.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.98

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	6 (33.3)	17 (42.5)
Number of Subjects Censored, n (%)	12 (66.7)	23 (57.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.95 (0.10, NE)	1.41 (0.69, 2.86)
Median (95% CI)	NE (0.95, NE)	NE (1.81, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.5*	0.6, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.158 (0.480)
95% CI		(0.452, 2.968)
Log-rank p-value		0.735

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	65.0 (42.0, 88.0)	59.9 (43.9, 75.8)
6 months	65.0 (42.0, 88.0)	51.4 (33.9, 69.0)
9 months	NE (NE, NE)	51.4 (33.9, 69.0)
12 months	NE (NE, NE)	51.4 (33.9, 69.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.32	2.84

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	6 (15.0)
Number of Subjects Censored, n (%)	17 (94.4)	34 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.66, NE)	NE (1.41, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	0.6, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.050 (1.085)
95% CI		(0.364, 25.582)
Log-rank p-value		0.283

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	84.4 (72.8, 95.9)
6 months	92.3 (77.8, 100.0)	84.4 (72.8, 95.9)
9 months	NE (NE, NE)	84.4 (72.8, 95.9)
12 months	NE (NE, NE)	84.4 (72.8, 95.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	2 (11.1)	3 (7.5)
Number of Subjects Censored, n (%)	16 (88.9)	37 (92.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.66, NE)	NE (5.55, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	0.7, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.448 (0.951)
95% CI		(0.069, 2.888)
Log-rank p-value		0.344

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (74.4, 100.0)	95.0 (88.2, 100.0)
6 months	88.9 (74.4, 100.0)	89.4 (77.0, 100.0)
9 months	NE (NE, NE)	89.4 (77.0, 100.0)
12 months	NE (NE, NE)	89.4 (77.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	3 (16.7)	3 (7.5)
Number of Subjects Censored, n (%)	15 (83.3)	37 (92.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.66, NE)	NE (6.54, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	1.0*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.291 (0.865)
95% CI		(0.053, 1.586)
Log-rank p-value		0.151

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.3 (66.1, 100.0)	94.4 (87.0, 100.0)
6 months	83.3 (66.1, 100.0)	94.4 (87.0, 100.0)
9 months	NE (NE, NE)	86.6 (70.3, 100.0)
12 months	NE (NE, NE)	86.6 (70.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	2 (11.1)	4 (10.0)
Number of Subjects Censored, n (%)	16 (88.9)	36 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	NE (3.68, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	0.7, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.738 (0.880)
95% CI		(0.131, 4.142)
Log-rank p-value		0.513

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (74.4, 100.0)	91.8 (83.0, 100.0)
6 months	88.9 (74.4, 100.0)	87.9 (76.4, 99.3)
9 months	NE (NE, NE)	87.9 (76.4, 99.3)
12 months	NE (NE, NE)	87.9 (76.4, 99.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	0
Number of Subjects Censored, n (%)	17 (94.4)	40 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.97, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	1.0*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.065

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	100.0 (100.0, 100.0)
6 months	92.3 (77.8, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	2 (11.1)	2 (5.0)
Number of Subjects Censored, n (%)	16 (88.9)	38 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.66, NE)	NE (4.86, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	1.0*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.225 (1.077)
95% CI		(0.027, 1.859)
Log-rank p-value		0.073

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (74.4, 100.0)	97.1 (91.6, 100.0)
6 months	88.9 (74.4, 100.0)	92.3 (81.6, 100.0)
9 months	NE (NE, NE)	92.3 (81.6, 100.0)
12 months	NE (NE, NE)	92.3 (81.6, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	2 (5.0)
Number of Subjects Censored, n (%)	18 (100.0)	38 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	0.7, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.402

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.9 (88.1, 100.0)
6 months	100.0 (100.0, 100.0)	94.9 (88.1, 100.0)
9 months	NE (NE, NE)	94.9 (88.1, 100.0)
12 months	NE (NE, NE)	94.9 (88.1, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.16

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	1 (2.5)
Number of Subjects Censored, n (%)	17 (94.4)	39 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.94, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	1.0*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.358 (1.440)
95% CI		(0.021, 6.013)
Log-rank p-value		0.510

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	96.6 (89.9, 100.0)
6 months	92.3 (77.8, 100.0)	96.6 (89.9, 100.0)
9 months	NE (NE, NE)	96.6 (89.9, 100.0)
12 months	NE (NE, NE)	96.6 (89.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.16

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	3 (16.7)	13 (32.5)
Number of Subjects Censored, n (%)	15 (83.3)	27 (67.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	1.58 (0.46, 11.53)
Median (95% CI)	NE (NE, NE)	11.53 (9.07, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (9.07, NE)
Min, Max	0.6, 5.6*	0.1, 12.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.702 (0.655)
95% CI		(0.472, 6.140)
Log-rank p-value		0.489

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.3 (66.1, 100.0)	74.7 (61.2, 88.3)
6 months	NE (NE, NE)	70.8 (55.9, 85.7)
9 months	NE (NE, NE)	70.8 (55.9, 85.7)
12 months	NE (NE, NE)	26.5 (0.0, 66.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.74	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	3 (7.5)
Number of Subjects Censored, n (%)	17 (94.4)	37 (92.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.72, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.373 (1.158)
95% CI		(0.142, 13.295)
Log-rank p-value		0.802

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (83.9, 100.0)	92.5 (84.3, 100.0)
6 months	94.4 (83.9, 100.0)	92.5 (84.3, 100.0)
9 months	NE (NE, NE)	92.5 (84.3, 100.0)
12 months	NE (NE, NE)	92.5 (84.3, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.16

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	3 (7.5)
Number of Subjects Censored, n (%)	17 (94.4)	37 (92.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.64, NE)	14.32 (4.30, NE)
Median (95% CI)	NE (NE, NE)	14.32 (14.32, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (14.32, NE)
Min, Max	1.6, 6.5*	0.6, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.708 (1.285)
95% CI		(0.057, 8.783)
Log-rank p-value		0.736

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (83.9, 100.0)	97.5 (92.7, 100.0)
6 months	94.4 (83.9, 100.0)	92.9 (82.9, 100.0)
9 months	NE (NE, NE)	92.9 (82.9, 100.0)
12 months	NE (NE, NE)	92.9 (82.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.44

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	5 (12.5)
Number of Subjects Censored, n (%)	18 (100.0)	35 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	11.53 (1.58, NE)
Median (95% CI)	NE (NE, NE)	NE (11.53, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (11.53, NE)
Min, Max	1.8*, 6.5*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.213

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	89.6 (80.0, 99.3)
6 months	100.0 (100.0, 100.0)	89.6 (80.0, 99.3)
9 months	NE (NE, NE)	89.6 (80.0, 99.3)
12 months	NE (NE, NE)	59.8 (11.5, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	2 (5.0)
Number of Subjects Censored, n (%)	17 (94.4)	38 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 5.6*	0.3, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.836 (1.229)
95% CI		(0.075, 9.308)
Log-rank p-value		0.865

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (83.9, 100.0)	95.0 (88.2, 100.0)
6 months	NE (NE, NE)	95.0 (88.2, 100.0)
9 months	NE (NE, NE)	95.0 (88.2, 100.0)
12 months	NE (NE, NE)	95.0 (88.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Vascular disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	2 (11.1)	19 (47.5)
Number of Subjects Censored, n (%)	16 (88.9)	21 (52.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	0.69 (0.23, 2.86)
Median (95% CI)	NE (NE, NE)	4.70 (1.61, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	0.0, 9.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.840 (0.747)
95% CI		(1.120, 20.918)
Log-rank p-value		0.021

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Vascular disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (74.4, 100.0)	54.8 (38.4, 71.2)
6 months	88.9 (74.4, 100.0)	46.0 (28.2, 63.9)
9 months	NE (NE, NE)	46.0 (28.2, 63.9)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	2.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	17 (42.5)
Number of Subjects Censored, n (%)	18 (100.0)	23 (57.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.84 (0.23, 2.96)
Median (95% CI)	NE (NE, NE)	NE (1.64, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	0.0, 9.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	60.6 (44.7, 76.5)
6 months	100.0 (100.0, 100.0)	50.9 (32.6, 69.2)
9 months	NE (NE, NE)	50.9 (32.6, 69.2)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	5 (27.8)	16 (40.0)
Number of Subjects Censored, n (%)	13 (72.2)	24 (60.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.03, NE)	1.61 (0.49, 5.03)
Median (95% CI)	NE (1.87, NE)	NE (2.27, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.2, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.387 (0.522)
95% CI		(0.498, 3.861)
Log-rank p-value		0.502

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	71.8 (50.8, 92.8)	63.4 (48.0, 78.8)
6 months	71.8 (50.8, 92.8)	53.5 (35.4, 71.7)
9 months	NE (NE, NE)	53.5 (35.4, 71.7)
12 months	NE (NE, NE)	53.5 (35.4, 71.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	6 (15.0)
Number of Subjects Censored, n (%)	17 (94.4)	34 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.87, NE)	NE (1.71, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	0.2, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.778 (1.088)
95% CI		(0.330, 23.421)
Log-rank p-value		0.299

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.1 (82.9, 100.0)	83.7 (71.6, 95.7)
6 months	94.1 (82.9, 100.0)	83.7 (71.6, 95.7)
9 months	NE (NE, NE)	83.7 (71.6, 95.7)
12 months	NE (NE, NE)	83.7 (71.6, 95.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	5 (12.5)
Number of Subjects Censored, n (%)	17 (94.4)	35 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.76, NE)	7.98 (2.27, NE)
Median (95% CI)	NE (NE, NE)	NE (7.98, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.8, 6.5*	0.4, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.859 (1.123)
95% CI		(0.206, 16.790)
Log-rank p-value		0.569

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (83.9, 100.0)	89.5 (79.7, 99.3)
6 months	94.4 (83.9, 100.0)	89.5 (79.7, 99.3)
9 months	NE (NE, NE)	74.6 (46.7, 100.0)
12 months	NE (NE, NE)	74.6 (46.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	5 (12.5)
Number of Subjects Censored, n (%)	17 (94.4)	35 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (5.03, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 6.5*	1.0*, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.767 (1.113)
95% CI		(0.200, 15.644)
Log-rank p-value		0.670

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (83.9, 100.0)	91.5 (82.1, 100.0)
6 months	94.4 (83.9, 100.0)	79.9 (62.9, 97.0)
9 months	NE (NE, NE)	79.9 (62.9, 97.0)
12 months	NE (NE, NE)	79.9 (62.9, 97.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	0
Number of Subjects Censored, n (%)	17 (94.4)	40 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.92, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.9, 6.5*	1.0*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.099

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (83.9, 100.0)	100.0 (100.0, 100.0)
6 months	94.4 (83.9, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	5 (27.8)	16 (40.0)
Number of Subjects Censored, n (%)	13 (72.2)	24 (60.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.61 (0.07, NE)	0.67 (0.39, 2.10)
Median (95% CI)	NE (1.61, NE)	NE (1.51, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.5*	0.1, 10.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.426 (0.517)
95% CI		(0.517, 3.930)
Log-rank p-value		0.511

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	72.2 (51.5, 92.9)	61.2 (45.7, 76.7)
6 months	72.2 (51.5, 92.9)	52.5 (31.8, 73.2)
9 months	NE (NE, NE)	52.5 (31.8, 73.2)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	2.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	11 (27.5)
Number of Subjects Censored, n (%)	18 (100.0)	29 (72.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	2.10 (0.46, NE)
Median (95% CI)	NE (NE, NE)	NE (5.19, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	0.1, 10.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.023

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	74.2 (60.3, 88.1)
6 months	100.0 (100.0, 100.0)	63.6 (41.0, 86.2)
9 months	NE (NE, NE)	63.6 (41.0, 86.2)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	1 (2.5)
Number of Subjects Censored, n (%)	18 (100.0)	39 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.564

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.5 (92.7, 100.0)
6 months	100.0 (100.0, 100.0)	97.5 (92.7, 100.0)
9 months	NE (NE, NE)	97.5 (92.7, 100.0)
12 months	NE (NE, NE)	97.5 (92.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	1 (2.5)
Number of Subjects Censored, n (%)	17 (94.4)	39 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.61, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.6, 6.5*	1.0*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.510 (1.427)
95% CI		(0.031, 8.361)
Log-rank p-value		0.608

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (83.9, 100.0)	97.3 (92.1, 100.0)
6 months	94.4 (83.9, 100.0)	97.3 (92.1, 100.0)
9 months	NE (NE, NE)	97.3 (92.1, 100.0)
12 months	NE (NE, NE)	97.3 (92.1, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.16

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	10 (25.0)
Number of Subjects Censored, n (%)	17 (94.4)	30 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	2.79 (0.46, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 6.5*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.907 (1.051)
95% CI		(0.625, 38.531)
Log-rank p-value		0.104

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (83.9, 100.0)	74.3 (60.4, 88.1)
6 months	94.4 (83.9, 100.0)	74.3 (60.4, 88.1)
9 months	NE (NE, NE)	74.3 (60.4, 88.1)
12 months	NE (NE, NE)	74.3 (60.4, 88.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	2.92

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	4 (10.0)
Number of Subjects Censored, n (%)	17 (94.4)	36 (90.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 6.5*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.931 (1.121)
95% CI		(0.215, 17.359)
Log-rank p-value		0.567

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (83.9, 100.0)	90.0 (80.7, 99.3)
6 months	94.4 (83.9, 100.0)	90.0 (80.7, 99.3)
9 months	NE (NE, NE)	90.0 (80.7, 99.3)
12 months	NE (NE, NE)	90.0 (80.7, 99.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	2 (5.0)
Number of Subjects Censored, n (%)	18 (100.0)	38 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.439

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.3 (86.4, 100.0)
6 months	100.0 (100.0, 100.0)	94.3 (86.4, 100.0)
9 months	NE (NE, NE)	94.3 (86.4, 100.0)
12 months	NE (NE, NE)	94.3 (86.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	2 (5.0)
Number of Subjects Censored, n (%)	18 (100.0)	38 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	0.5, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.343

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.0 (88.2, 100.0)
6 months	100.0 (100.0, 100.0)	95.0 (88.2, 100.0)
9 months	NE (NE, NE)	95.0 (88.2, 100.0)
12 months	NE (NE, NE)	95.0 (88.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	6 (33.3)	8 (20.0)
Number of Subjects Censored, n (%)	12 (66.7)	32 (80.0)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.62, NE)	NE (0.95, NE)
Median (95% CI)	NE (1.87, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 6.5*	0.1, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.672 (0.577)
95% CI		(0.217, 2.079)
Log-rank p-value		0.537

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	64.6 (41.5, 87.8)	79.1 (66.2, 92.1)
6 months	64.6 (41.5, 87.8)	79.1 (66.2, 92.1)
9 months	NE (NE, NE)	79.1 (66.2, 92.1)
12 months	NE (NE, NE)	79.1 (66.2, 92.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.42

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	3 (16.7)	6 (15.0)
Number of Subjects Censored, n (%)	15 (83.3)	34 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	NE (1.97, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.0, 6.5*	0.7, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.856 (0.710)
95% CI		(0.213, 3.441)
Log-rank p-value		0.838

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.0 (65.4, 100.0)	84.2 (72.5, 95.9)
6 months	83.0 (65.4, 100.0)	84.2 (72.5, 95.9)
9 months	NE (NE, NE)	84.2 (72.5, 95.9)
12 months	NE (NE, NE)	84.2 (72.5, 95.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	0
Number of Subjects Censored, n (%)	17 (94.4)	40 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.62, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.6, 6.5*	1.0*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.083

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.4 (83.9, 100.0)	100.0 (100.0, 100.0)
6 months	94.4 (83.9, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	8 (20.0)
Number of Subjects Censored, n (%)	17 (94.4)	32 (80.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	11.53 (1.97, NE)
Median (95% CI)	NE (4.34, NE)	NE (11.53, NE)
75% percentile (95% CI)	NE (4.34, NE)	NE (11.53, NE)
Min, Max	1.8*, 6.5*	0.2, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.521 (1.085)
95% CI		(0.301, 21.118)
Log-rank p-value		0.283

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	83.8 (71.9, 95.7)
6 months	80.0 (44.9, 100.0)	83.8 (71.9, 95.7)
9 months	NE (NE, NE)	75.4 (56.5, 94.4)
12 months	NE (NE, NE)	50.3 (8.1, 92.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.10

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	3 (7.5)
Number of Subjects Censored, n (%)	18 (100.0)	37 (92.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (6.28, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	1.0*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.203

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.3 (86.6, 100.0)
6 months	100.0 (100.0, 100.0)	94.3 (86.6, 100.0)
9 months	NE (NE, NE)	85.7 (68.2, 100.0)
12 months	NE (NE, NE)	85.7 (68.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	2 (5.0)
Number of Subjects Censored, n (%)	17 (94.4)	38 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	11.56 (11.56, NE)
Median (95% CI)	NE (4.34, NE)	NE (11.56, NE)
75% percentile (95% CI)	NE (4.34, NE)	NE (11.56, NE)
Min, Max	1.8*, 6.5*	1.0*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.332 (1.417)
95% CI		(0.021, 5.337)
Log-rank p-value		0.414

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.1 (91.6, 100.0)
6 months	80.0 (44.9, 100.0)	97.1 (91.6, 100.0)
9 months	NE (NE, NE)	97.1 (91.6, 100.0)
12 months	NE (NE, NE)	64.8 (12.8, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.16

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	1 (2.5)
Number of Subjects Censored, n (%)	18 (100.0)	39 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	0.7, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.544

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.5 (92.7, 100.0)
6 months	100.0 (100.0, 100.0)	97.5 (92.7, 100.0)
9 months	NE (NE, NE)	97.5 (92.7, 100.0)
12 months	NE (NE, NE)	97.5 (92.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	2 (11.1)	6 (15.0)
Number of Subjects Censored, n (%)	16 (88.9)	34 (85.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.69, NE)	6.41 (2.96, NE)
Median (95% CI)	NE (NE, NE)	NE (6.41, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	0.1, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.772 (0.852)
95% CI		(0.145, 4.105)
Log-rank p-value		0.819

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (74.4, 100.0)	91.2 (81.4, 100.0)
6 months	88.9 (74.4, 100.0)	79.0 (60.8, 97.2)
9 months	NE (NE, NE)	70.2 (47.3, 93.1)
12 months	NE (NE, NE)	70.2 (47.3, 93.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	3 (7.5)
Number of Subjects Censored, n (%)	18 (100.0)	37 (92.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.78, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	1.0*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.443

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
6 months	100.0 (100.0, 100.0)	88.9 (74.2, 100.0)
9 months	NE (NE, NE)	81.5 (62.1, 100.0)
12 months	NE (NE, NE)	81.5 (62.1, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	3 (7.5)
Number of Subjects Censored, n (%)	18 (100.0)	37 (92.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.96, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	0.1, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.310

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	91.2 (81.4, 100.0)
6 months	100.0 (100.0, 100.0)	91.2 (81.4, 100.0)
9 months	NE (NE, NE)	91.2 (81.4, 100.0)
12 months	NE (NE, NE)	91.2 (81.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.70

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Endocrine disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	10 (25.0)
Number of Subjects Censored, n (%)	18 (100.0)	30 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	6.01 (1.84, NE)
Median (95% CI)	NE (NE, NE)	NE (6.01, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (6.90, NE)
Min, Max	1.8*, 6.5*	0.6, 12.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.038

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Endocrine disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	80.7 (67.8, 93.6)
6 months	100.0 (100.0, 100.0)	75.9 (60.8, 91.1)
9 months	NE (NE, NE)	55.2 (26.7, 83.7)
12 months	NE (NE, NE)	55.2 (26.7, 83.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	10 (25.0)
Number of Subjects Censored, n (%)	18 (100.0)	30 (75.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	6.01 (1.84, NE)
Median (95% CI)	NE (NE, NE)	NE (6.01, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (6.90, NE)
Min, Max	1.8*, 6.5*	0.6, 12.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.038

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	80.7 (67.8, 93.6)
6 months	100.0 (100.0, 100.0)	75.9 (60.8, 91.1)
9 months	NE (NE, NE)	55.2 (26.7, 83.7)
12 months	NE (NE, NE)	55.2 (26.7, 83.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	3.65

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	3 (16.7)	2 (5.0)
Number of Subjects Censored, n (%)	15 (83.3)	38 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.72, NE)	NE (NE, NE)
Median (95% CI)	NE (2.14, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.301 (0.932)
95% CI		(0.048, 1.867)
Log-rank p-value		0.175

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.9 (59.3, 100.0)	93.8 (85.2, 100.0)
6 months	79.9 (59.3, 100.0)	93.8 (85.2, 100.0)
9 months	NE (NE, NE)	93.8 (85.2, 100.0)
12 months	NE (NE, NE)	93.8 (85.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.81	3.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	2 (11.1)	1 (2.5)
Number of Subjects Censored, n (%)	16 (88.9)	39 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.72, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.7, 6.5*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.248 (1.235)
95% CI		(0.022, 2.788)
Log-rank p-value		0.239

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.2 (70.4, 100.0)	97.5 (92.7, 100.0)
6 months	87.2 (70.4, 100.0)	97.5 (92.7, 100.0)
9 months	NE (NE, NE)	97.5 (92.7, 100.0)
12 months	NE (NE, NE)	97.5 (92.7, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.16

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	1 (2.5)
Number of Subjects Censored, n (%)	18 (100.0)	39 (97.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	1.0*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.584

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.3 (89.2, 100.0)
6 months	100.0 (100.0, 100.0)	96.3 (89.2, 100.0)
9 months	NE (NE, NE)	96.3 (89.2, 100.0)
12 months	NE (NE, NE)	96.3 (89.2, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.16

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	1 (5.6)	0
Number of Subjects Censored, n (%)	17 (94.4)	40 (100.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.94, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	1.0*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.221

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.3 (77.8, 100.0)	100.0 (100.0, 100.0)
6 months	92.3 (77.8, 100.0)	100.0 (100.0, 100.0)
9 months	NE (NE, NE)	100.0 (100.0, 100.0)
12 months	NE (NE, NE)	100.0 (100.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	2 (11.1)	5 (12.5)
Number of Subjects Censored, n (%)	16 (88.9)	35 (87.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (0.95, NE)	9.66 (5.55, NE)
Median (95% CI)	NE (NE, NE)	NE (9.66, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (9.66, NE)
Min, Max	1.0, 6.5*	0.6, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.592 (0.883)
95% CI		(0.105, 3.346)
Log-rank p-value		0.505

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (74.4, 100.0)	92.2 (83.7, 100.0)
6 months	88.9 (74.4, 100.0)	86.4 (72.9, 100.0)
9 months	NE (NE, NE)	86.4 (72.9, 100.0)
12 months	NE (NE, NE)	57.6 (10.6, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.14

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	2 (5.0)
Number of Subjects Censored, n (%)	18 (100.0)	38 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	9.66 (9.66, NE)
Median (95% CI)	NE (NE, NE)	NE (9.66, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (9.66, NE)
Min, Max	1.8*, 6.5*	1.0*, 15.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.588

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.1 (91.6, 100.0)
6 months	100.0 (100.0, 100.0)	97.1 (91.6, 100.0)
9 months	NE (NE, NE)	97.1 (91.6, 100.0)
12 months	NE (NE, NE)	64.8 (12.8, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.16

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Number of Subjects with Events, n (%)	0	2 (5.0)
Number of Subjects Censored, n (%)	18 (100.0)	38 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.55, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	1.8*, 6.5*	0.7, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.544

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
Regorafenib

Statistics	Placebo + BSC N=18	Fruquintinib + BSC N=40
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.5 (92.7, 100.0)
6 months	100.0 (100.0, 100.0)	91.8 (79.9, 100.0)
9 months	NE (NE, NE)	91.8 (79.9, 100.0)
12 months	NE (NE, NE)	91.8 (79.9, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.83	4.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	54 (59.3)	122 (68.2)
Number of Subjects Censored, n (%)	37 (40.7)	57 (31.8)
Time to first TEAE (months)		
25% percentile (95% CI)	0.46 (0.16, 0.69)	0.49 (0.30, 0.69)
Median (95% CI)	1.64 (0.76, 3.22)	1.48 (0.95, 2.43)
75% percentile (95% CI)	NE (3.22, NE)	6.47 (4.37, NE)
Min, Max	0.0, 6.4*	0.0, 12.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.015 (0.167)
95% CI		(0.732, 1.408)
Log-rank p-value		0.980

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	40.8 (30.2, 51.3)	39.8 (32.5, 47.1)
6 months	28.5 (12.2, 44.9)	25.8 (18.1, 33.6)
9 months	NE (NE, NE)	19.3 (8.7, 29.9)
12 months	NE (NE, NE)	19.3 (8.7, 29.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.38	1.45

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	23 (25.3)	55 (30.7)
Number of Subjects Censored, n (%)	68 (74.7)	124 (69.3)
Time to first TEAE (months)		
25% percentile (95% CI)	3.22 (0.72, NE)	1.74 (0.95, 3.68)
Median (95% CI)	NE (4.70, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.028 (0.251)
95% CI		(0.628, 1.682)
Log-rank p-value		0.920

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.4 (66.1, 84.8)	70.9 (64.1, 77.8)
6 months	60.9 (40.9, 81.0)	66.9 (59.3, 74.5)
9 months	NE (NE, NE)	64.7 (56.3, 73.2)
12 months	NE (NE, NE)	64.7 (56.3, 73.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.30	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	13 (14.3)	33 (18.4)
Number of Subjects Censored, n (%)	78 (85.7)	146 (81.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.68, NE)	NE (3.32, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.221 (0.341)
95% CI		(0.626, 2.381)
Log-rank p-value		0.595

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	84.4 (76.6, 92.3)	82.6 (76.9, 88.3)
6 months	84.4 (76.6, 92.3)	79.8 (73.4, 86.1)
9 months	NE (NE, NE)	79.8 (73.4, 86.1)
12 months	NE (NE, NE)	79.8 (73.4, 86.1)
18 months	NE (NE, NE)	79.8 (73.4, 86.1)
Median Follow-up Time (months)	2.46	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	10 (11.0)	23 (12.8)
Number of Subjects Censored, n (%)	81 (89.0)	156 (87.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.70, NE)	NE (6.11, NE)
Median (95% CI)	NE (4.70, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.838 (0.392)
95% CI		(0.389, 1.807)
Log-rank p-value		0.640

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.7 (81.5, 95.9)	90.8 (86.5, 95.1)
6 months	77.6 (56.3, 98.9)	85.5 (79.3, 91.6)
9 months	NE (NE, NE)	81.4 (73.3, 89.4)
12 months	NE (NE, NE)	81.4 (73.3, 89.4)
18 months	NE (NE, NE)	81.4 (73.3, 89.4)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	2 (2.2)	17 (9.5)
Number of Subjects Censored, n (%)	89 (97.8)	162 (90.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.1, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.927 (0.749)
95% CI		(0.905, 17.050)
Log-rank p-value		0.049

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (93.7, 100.0)	90.8 (86.5, 95.1)
6 months	97.3 (93.7, 100.0)	89.6 (84.8, 94.4)
9 months	NE (NE, NE)	89.6 (84.8, 94.4)
12 months	NE (NE, NE)	89.6 (84.8, 94.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	12 (13.2)	10 (5.6)
Number of Subjects Censored, n (%)	79 (86.8)	169 (94.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.75, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.232 (0.461)
95% CI		(0.094, 0.573)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.0 (79.8, 94.2)	97.6 (95.3, 99.9)
6 months	80.8 (67.3, 94.3)	91.6 (85.9, 97.4)
9 months	NE (NE, NE)	91.6 (85.9, 97.4)
12 months	NE (NE, NE)	91.6 (85.9, 97.4)
18 months	NE (NE, NE)	76.4 (48.6, 100.0)
Median Follow-up Time (months)	2.79	4.37

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	8 (8.8)	6 (3.4)
Number of Subjects Censored, n (%)	83 (91.2)	173 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.332 (0.542)
95% CI		(0.115, 0.958)
Log-rank p-value		0.032

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.8 (84.6, 96.9)	96.4 (93.5, 99.2)
6 months	90.8 (84.6, 96.9)	96.4 (93.5, 99.2)
9 months	NE (NE, NE)	96.4 (93.5, 99.2)
12 months	NE (NE, NE)	96.4 (93.5, 99.2)
18 months	NE (NE, NE)	96.4 (93.5, 99.2)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	10 (5.6)
Number of Subjects Censored, n (%)	90 (98.9)	169 (94.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.72, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.971 (1.068)
95% CI		(0.366, 24.091)
Log-rank p-value		0.307

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.7, 100.0)	97.1 (94.6, 99.6)
6 months	98.9 (96.7, 100.0)	93.0 (88.3, 97.7)
9 months	NE (NE, NE)	93.0 (88.3, 97.7)
12 months	NE (NE, NE)	84.5 (68.2, 100.0)
18 months	NE (NE, NE)	84.5 (68.2, 100.0)
Median Follow-up Time (months)	2.79	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	2 (2.2)	5 (2.8)
Number of Subjects Censored, n (%)	89 (97.8)	174 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.944 (0.849)
95% CI		(0.179, 4.985)
Log-rank p-value		0.947

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (94.7, 100.0)	97.6 (95.2, 99.9)
6 months	97.8 (94.7, 100.0)	96.4 (93.2, 99.6)
9 months	NE (NE, NE)	96.4 (93.2, 99.6)
12 months	NE (NE, NE)	96.4 (93.2, 99.6)
18 months	NE (NE, NE)	96.4 (93.2, 99.6)
Median Follow-up Time (months)	2.79	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	5 (2.8)
Number of Subjects Censored, n (%)	91 (100.0)	174 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.175

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.3 (96.4, 100.0)
6 months	100.0 (100.0, 100.0)	95.4 (90.7, 100.0)
9 months	NE (NE, NE)	95.4 (90.7, 100.0)
12 months	NE (NE, NE)	95.4 (90.7, 100.0)
18 months	NE (NE, NE)	95.4 (90.7, 100.0)
Median Follow-up Time (months)	2.79	3.98

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	47 (51.6)	121 (67.6)
Number of Subjects Censored, n (%)	44 (48.4)	58 (32.4)
Time to first TEAE (months)		
25% percentile (95% CI)	0.59 (0.30, 1.08)	0.39 (0.26, 0.56)
Median (95% CI)	2.27 (1.45, 5.36)	1.35 (0.72, 1.87)
75% percentile (95% CI)	5.36 (4.34, NE)	5.55 (3.75, NE)
Min, Max	0.0, 6.4*	0.0, 11.2*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.299 (0.175)
95% CI		(0.921, 1.831)
Log-rank p-value		0.124

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	42.1 (28.7, 55.4)	37.7 (30.4, 45.0)
6 months	15.8 (0.0, 39.9)	23.5 (15.1, 31.8)
9 months	NE (NE, NE)	23.5 (15.1, 31.8)
12 months	NE (NE, NE)	NE (NE, NE)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.54	1.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	10 (11.0)	46 (25.7)
Number of Subjects Censored, n (%)	81 (89.0)	133 (74.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.39 (1.41, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 12.3*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.137 (0.351)
95% CI		(1.073, 4.254)
Log-rank p-value		0.029

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.4 (81.6, 95.2)	76.4 (70.0, 82.7)
6 months	88.4 (81.6, 95.2)	71.9 (64.0, 79.7)
9 months	NE (NE, NE)	66.6 (56.4, 76.7)
12 months	NE (NE, NE)	66.6 (56.4, 76.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	15 (16.5)	31 (17.3)
Number of Subjects Censored, n (%)	76 (83.5)	148 (82.7)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (2.79, NE)	NE (3.58, NE)
Median (95% CI)	NE (4.34, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.989 (0.325)
95% CI		(0.523, 1.869)
Log-rank p-value		0.938

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.6 (75.6, 91.7)	83.1 (77.4, 88.7)
6 months	73.2 (52.8, 93.6)	81.2 (75.1, 87.3)
9 months	NE (NE, NE)	81.2 (75.1, 87.3)
12 months	NE (NE, NE)	81.2 (75.1, 87.3)
18 months	NE (NE, NE)	81.2 (75.1, 87.3)
Median Follow-up Time (months)	2.60	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	13 (14.3)	30 (16.8)
Number of Subjects Censored, n (%)	78 (85.7)	149 (83.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.92, NE)	NE (3.71, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.959 (0.348)
95% CI		(0.485, 1.895)
Log-rank p-value		0.896

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.8 (71.3, 92.4)	85.8 (80.3, 91.3)
6 months	81.8 (71.3, 92.4)	79.1 (71.8, 86.4)
9 months	NE (NE, NE)	76.9 (68.5, 85.2)
12 months	NE (NE, NE)	76.9 (68.5, 85.2)
18 months	NE (NE, NE)	76.9 (68.5, 85.2)
Median Follow-up Time (months)	2.79	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	6 (6.6)	40 (22.3)
Number of Subjects Censored, n (%)	85 (93.4)	139 (77.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.92, NE)	5.82 (2.76, NE)
Median (95% CI)	NE (NE, NE)	NE (9.33, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.096 (0.479)
95% CI		(1.210, 7.922)
Log-rank p-value		0.013

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.2 (79.0, 99.5)	80.8 (74.8, 86.9)
6 months	89.2 (79.0, 99.5)	73.9 (66.0, 81.8)
9 months	NE (NE, NE)	69.8 (59.0, 80.6)
12 months	NE (NE, NE)	62.8 (46.6, 79.0)
18 months	NE (NE, NE)	62.8 (46.6, 79.0)
Median Follow-up Time (months)	2.79	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	10 (11.0)	26 (14.5)
Number of Subjects Censored, n (%)	81 (89.0)	153 (85.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (5.36, NE)	10.18 (5.22, NE)
Median (95% CI)	NE (5.36, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.2, 8.4*	0.0, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.851 (0.386)
95% CI		(0.399, 1.814)
Log-rank p-value		0.652

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.9 (81.9, 95.9)	89.8 (85.2, 94.4)
6 months	76.2 (52.4, 100.0)	82.7 (75.7, 89.7)
9 months	NE (NE, NE)	80.7 (72.9, 88.6)
12 months	NE (NE, NE)	73.4 (57.9, 88.9)
18 months	NE (NE, NE)	73.4 (57.9, 88.9)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	5 (5.5)	36 (20.1)
Number of Subjects Censored, n (%)	86 (94.5)	143 (79.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (2.00, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.589 (0.479)
95% CI		(1.403, 9.179)
Log-rank p-value		0.004

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.8 (88.5, 99.1)	80.4 (74.4, 86.3)
6 months	93.8 (88.5, 99.1)	78.0 (71.3, 84.7)
9 months	NE (NE, NE)	78.0 (71.3, 84.7)
12 months	NE (NE, NE)	78.0 (71.3, 84.7)
18 months	NE (NE, NE)	78.0 (71.3, 84.7)
Median Follow-up Time (months)	2.79	3.15

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	5 (5.5)	9 (5.0)
Number of Subjects Censored, n (%)	86 (94.5)	170 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.681 (0.572)
95% CI		(0.222, 2.092)
Log-rank p-value		0.511

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.9 (88.7, 99.1)	96.5 (93.8, 99.3)
6 months	93.9 (88.7, 99.1)	93.5 (89.2, 97.8)
9 months	NE (NE, NE)	93.5 (89.2, 97.8)
12 months	NE (NE, NE)	93.5 (89.2, 97.8)
18 months	NE (NE, NE)	93.5 (89.2, 97.8)
Median Follow-up Time (months)	2.73	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	5 (2.8)
Number of Subjects Censored, n (%)	91 (100.0)	174 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.205

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.7 (95.5, 99.9)
6 months	100.0 (100.0, 100.0)	96.1 (92.3, 99.9)
9 months	NE (NE, NE)	96.1 (92.3, 99.9)
12 months	NE (NE, NE)	96.1 (92.3, 99.9)
18 months	NE (NE, NE)	96.1 (92.3, 99.9)
Median Follow-up Time (months)	2.79	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	2 (2.2)	5 (2.8)
Number of Subjects Censored, n (%)	89 (97.8)	174 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.147 (0.837)
95% CI		(0.222, 5.923)
Log-rank p-value		0.870

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (94.1, 100.0)	97.1 (94.7, 99.6)
6 months	97.5 (94.1, 100.0)	97.1 (94.7, 99.6)
9 months	NE (NE, NE)	97.1 (94.7, 99.6)
12 months	NE (NE, NE)	97.1 (94.7, 99.6)
18 months	NE (NE, NE)	97.1 (94.7, 99.6)
Median Follow-up Time (months)	2.79	3.98

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	3 (3.3)	1 (0.6)
Number of Subjects Censored, n (%)	88 (96.7)	178 (99.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.139 (1.158)
95% CI		(0.014, 1.348)
Log-rank p-value		0.057

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.2 (92.0, 100.0)	99.4 (98.2, 100.0)
6 months	96.2 (92.0, 100.0)	99.4 (98.2, 100.0)
9 months	NE (NE, NE)	99.4 (98.2, 100.0)
12 months	NE (NE, NE)	99.4 (98.2, 100.0)
18 months	NE (NE, NE)	99.4 (98.2, 100.0)
Median Follow-up Time (months)	2.79	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	4 (2.2)
Number of Subjects Censored, n (%)	91 (100.0)	175 (97.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.175

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.6 (95.2, 99.9)
6 months	100.0 (100.0, 100.0)	97.6 (95.2, 99.9)
9 months	NE (NE, NE)	97.6 (95.2, 99.9)
12 months	NE (NE, NE)	97.6 (95.2, 99.9)
18 months	NE (NE, NE)	97.6 (95.2, 99.9)
Median Follow-up Time (months)	2.79	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	31 (34.1)	85 (47.5)
Number of Subjects Censored, n (%)	60 (65.9)	94 (52.5)
Time to first TEAE (months)		
25% percentile (95% CI)	0.99 (0.69, 2.04)	1.15 (0.72, 1.64)
Median (95% CI)	NE (4.27, NE)	5.49 (2.86, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.181 (0.215)
95% CI		(0.774, 1.801)
Log-rank p-value		0.464

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	64.8 (54.5, 75.1)	55.8 (48.2, 63.4)
6 months	54.0 (32.9, 75.2)	49.2 (41.0, 57.4)
9 months	NE (NE, NE)	44.0 (34.9, 53.2)
12 months	NE (NE, NE)	44.0 (34.9, 53.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	22 (24.2)	55 (30.7)
Number of Subjects Censored, n (%)	69 (75.8)	124 (69.3)
Time to first TEAE (months)		
25% percentile (95% CI)	4.27 (0.99, NE)	1.94 (1.15, 3.58)
Median (95% CI)	NE (4.27, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.125 (0.260)
95% CI		(0.676, 1.872)
Log-rank p-value		0.693

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	75.0 (65.6, 84.4)	71.0 (64.0, 77.9)
6 months	65.6 (46.6, 84.7)	64.8 (56.8, 72.8)
9 months	NE (NE, NE)	64.8 (56.8, 72.8)
12 months	NE (NE, NE)	64.8 (56.8, 72.8)
18 months	NE (NE, NE)	64.8 (56.8, 72.8)
Median Follow-up Time (months)	2.30	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	15 (8.4)
Number of Subjects Censored, n (%)	90 (98.9)	164 (91.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		>999 (>999)
95% CI		(0.000, NE)
Log-rank p-value		0.018

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.6, 100.0)	91.8 (87.7, 95.9)
6 months	98.9 (96.6, 100.0)	90.8 (86.3, 95.3)
9 months	NE (NE, NE)	90.8 (86.3, 95.3)
12 months	NE (NE, NE)	90.8 (86.3, 95.3)
18 months	NE (NE, NE)	90.8 (86.3, 95.3)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	3 (3.3)	13 (7.3)
Number of Subjects Censored, n (%)	88 (96.7)	166 (92.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 6.8*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.570 (0.652)
95% CI		(0.437, 5.638)
Log-rank p-value		0.484

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.6 (92.8, 100.0)	94.0 (90.4, 97.6)
6 months	96.6 (92.8, 100.0)	91.8 (87.1, 96.5)
9 months	NE (NE, NE)	87.9 (79.3, 96.5)
12 months	NE (NE, NE)	87.9 (79.3, 96.5)
18 months	NE (NE, NE)	87.9 (79.3, 96.5)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	4 (4.4)	3 (1.7)
Number of Subjects Censored, n (%)	87 (95.6)	176 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.324 (0.766)
95% CI		(0.072, 1.455)
Log-rank p-value		0.113

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.9 (90.0, 99.9)	98.2 (96.1, 100.0)
6 months	94.9 (90.0, 99.9)	98.2 (96.1, 100.0)
9 months	NE (NE, NE)	98.2 (96.1, 100.0)
12 months	NE (NE, NE)	98.2 (96.1, 100.0)
18 months	NE (NE, NE)	98.2 (96.1, 100.0)
Median Follow-up Time (months)	2.79	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	5 (2.8)
Number of Subjects Censored, n (%)	90 (98.9)	174 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.397 (1.143)
95% CI		(0.149, 13.133)
Log-rank p-value		0.737

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.6, 100.0)	97.6 (95.3, 99.9)
6 months	98.9 (96.6, 100.0)	97.6 (95.3, 99.9)
9 months	NE (NE, NE)	93.4 (84.9, 100.0)
12 months	NE (NE, NE)	93.4 (84.9, 100.0)
18 months	NE (NE, NE)	93.4 (84.9, 100.0)
Median Follow-up Time (months)	2.79	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	7 (3.9)
Number of Subjects Censored, n (%)	91 (100.0)	172 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.072

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.8 (92.7, 98.8)
6 months	100.0 (100.0, 100.0)	95.8 (92.7, 98.8)
9 months	NE (NE, NE)	95.8 (92.7, 98.8)
12 months	NE (NE, NE)	95.8 (92.7, 98.8)
18 months	NE (NE, NE)	95.8 (92.7, 98.8)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	7 (3.9)
Number of Subjects Censored, n (%)	91 (100.0)	172 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.094

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.4 (93.7, 99.2)
6 months	100.0 (100.0, 100.0)	96.4 (93.7, 99.2)
9 months	NE (NE, NE)	94.3 (89.3, 99.3)
12 months	NE (NE, NE)	94.3 (89.3, 99.3)
18 months	NE (NE, NE)	94.3 (89.3, 99.3)
Median Follow-up Time (months)	2.79	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	2 (2.2)	4 (2.2)
Number of Subjects Censored, n (%)	89 (97.8)	175 (97.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.608 (0.918)
95% CI		(0.100, 3.678)
Log-rank p-value		0.591

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (94.6, 100.0)	98.8 (97.3, 100.0)
6 months	97.7 (94.6, 100.0)	97.2 (93.6, 100.0)
9 months	NE (NE, NE)	95.2 (89.9, 100.0)
12 months	NE (NE, NE)	95.2 (89.9, 100.0)
18 months	NE (NE, NE)	95.2 (89.9, 100.0)
Median Follow-up Time (months)	2.79	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	4 (2.2)
Number of Subjects Censored, n (%)	90 (98.9)	175 (97.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.638 (1.121)
95% CI		(0.182, 14.749)
Log-rank p-value		0.647

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.5, 100.0)	97.4 (94.9, 99.9)
6 months	98.8 (96.5, 100.0)	97.4 (94.9, 99.9)
9 months	NE (NE, NE)	97.4 (94.9, 99.9)
12 months	NE (NE, NE)	97.4 (94.9, 99.9)
18 months	NE (NE, NE)	97.4 (94.9, 99.9)
Median Follow-up Time (months)	2.79	3.98

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	2 (1.1)
Number of Subjects Censored, n (%)	91 (100.0)	177 (98.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.438

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.4 (98.3, 100.0)
6 months	100.0 (100.0, 100.0)	98.4 (96.1, 100.0)
9 months	NE (NE, NE)	98.4 (96.1, 100.0)
12 months	NE (NE, NE)	98.4 (96.1, 100.0)
18 months	NE (NE, NE)	98.4 (96.1, 100.0)
Median Follow-up Time (months)	2.79	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	26 (28.6)	72 (40.2)
Number of Subjects Censored, n (%)	65 (71.4)	107 (59.8)
Time to first TEAE (months)		
25% percentile (95% CI)	1.68 (0.95, NE)	1.54 (0.95, 1.91)
Median (95% CI)	5.82 (5.82, NE)	NE (4.73, NE)
75% percentile (95% CI)	NE (5.82, NE)	NE (NE, NE)
Min, Max	0.4*, 6.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.241 (0.236)
95% CI		(0.782, 1.969)
Log-rank p-value		0.398

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	69.5 (59.3, 79.7)	63.0 (55.7, 70.3)
6 months	46.3 (8.6, 84.0)	56.5 (48.2, 64.8)
9 months	NE (NE, NE)	51.1 (41.6, 60.6)
12 months	NE (NE, NE)	51.1 (41.6, 60.6)
18 months	NE (NE, NE)	51.1 (41.6, 60.6)
Median Follow-up Time (months)	2.17	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	9 (9.9)	22 (12.3)
Number of Subjects Censored, n (%)	82 (90.1)	157 (87.7)
Time to first TEAE (months)		
25% percentile (95% CI)	5.82 (5.82, NE)	NE (6.47, NE)
Median (95% CI)	NE (5.82, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (5.82, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.992 (0.424)
95% CI		(0.432, 2.274)
Log-rank p-value		0.992

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.4 (80.7, 96.1)	89.7 (85.0, 94.4)
6 months	66.3 (28.4, 100.0)	85.1 (78.8, 91.4)
9 months	NE (NE, NE)	83.1 (75.8, 90.4)
12 months	NE (NE, NE)	83.1 (75.8, 90.4)
18 months	NE (NE, NE)	83.1 (75.8, 90.4)
Median Follow-up Time (months)	2.73	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	4 (4.4)	12 (6.7)
Number of Subjects Censored, n (%)	87 (95.6)	167 (93.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.197 (0.586)
95% CI		(0.379, 3.777)
Log-rank p-value		0.776

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.2 (90.6, 99.8)	93.1 (89.1, 97.1)
6 months	95.2 (90.6, 99.8)	93.1 (89.1, 97.1)
9 months	NE (NE, NE)	89.4 (81.3, 97.5)
12 months	NE (NE, NE)	89.4 (81.3, 97.5)
18 months	NE (NE, NE)	89.4 (81.3, 97.5)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	2 (2.2)	13 (7.3)
Number of Subjects Censored, n (%)	89 (97.8)	166 (92.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.571 (0.765)
95% CI		(0.574, 11.520)
Log-rank p-value		0.219

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (94.5, 100.0)	93.4 (89.7, 97.2)
6 months	97.7 (94.5, 100.0)	92.4 (88.2, 96.6)
9 months	NE (NE, NE)	88.7 (80.6, 96.9)
12 months	NE (NE, NE)	88.7 (80.6, 96.9)
18 months	NE (NE, NE)	88.7 (80.6, 96.9)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	3 (3.3)	19 (10.6)
Number of Subjects Censored, n (%)	88 (96.7)	160 (89.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.585 (0.624)
95% CI		(0.760, 8.790)
Log-rank p-value		0.121

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.6 (92.7, 100.0)	90.4 (86.0, 94.9)
6 months	96.6 (92.7, 100.0)	87.3 (81.7, 92.9)
9 months	NE (NE, NE)	87.3 (81.7, 92.9)
12 months	NE (NE, NE)	87.3 (81.7, 92.9)
18 months	NE (NE, NE)	87.3 (81.7, 92.9)
Median Follow-up Time (months)	2.79	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	18 (10.1)
Number of Subjects Censored, n (%)	90 (98.9)	161 (89.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		6.453 (1.034)
95% CI		(0.851, 48.960)
Log-rank p-value		0.046

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	90.9 (86.5, 95.3)
6 months	92.9 (79.4, 100.0)	87.9 (81.9, 93.9)
9 months	NE (NE, NE)	86.0 (79.2, 92.9)
12 months	NE (NE, NE)	86.0 (79.2, 92.9)
18 months	NE (NE, NE)	86.0 (79.2, 92.9)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	5 (5.5)	9 (5.0)
Number of Subjects Censored, n (%)	86 (94.5)	170 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.762 (0.562)
95% CI		(0.254, 2.293)
Log-rank p-value		0.629

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.8 (86.6, 99.0)	94.4 (90.9, 98.0)
6 months	92.8 (86.6, 99.0)	94.4 (90.9, 98.0)
9 months	NE (NE, NE)	94.4 (90.9, 98.0)
12 months	NE (NE, NE)	94.4 (90.9, 98.0)
18 months	NE (NE, NE)	94.4 (90.9, 98.0)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	13 (7.3)
Number of Subjects Censored, n (%)	91 (100.0)	166 (92.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.026

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.6 (90.0, 97.3)
6 months	100.0 (100.0, 100.0)	91.4 (86.7, 96.1)
9 months	NE (NE, NE)	91.4 (86.7, 96.1)
12 months	NE (NE, NE)	91.4 (86.7, 96.1)
18 months	NE (NE, NE)	91.4 (86.7, 96.1)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	3 (3.3)	5 (2.8)
Number of Subjects Censored, n (%)	88 (96.7)	174 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.572 (0.754)
95% CI		(0.130, 2.510)
Log-rank p-value		0.388

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.0 (91.5, 100.0)	98.3 (96.3, 100.0)
6 months	96.0 (91.5, 100.0)	96.7 (93.0, 100.0)
9 months	NE (NE, NE)	94.7 (89.5, 99.9)
12 months	NE (NE, NE)	94.7 (89.5, 99.9)
18 months	NE (NE, NE)	94.7 (89.5, 99.9)
Median Follow-up Time (months)	2.79	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	8 (4.5)
Number of Subjects Censored, n (%)	91 (100.0)	171 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.068

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	95.8 (92.8, 98.9)
6 months	100.0 (100.0, 100.0)	94.6 (90.8, 98.4)
9 months	NE (NE, NE)	94.6 (90.8, 98.4)
12 months	NE (NE, NE)	94.6 (90.8, 98.4)
18 months	NE (NE, NE)	94.6 (90.8, 98.4)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	7 (3.9)
Number of Subjects Censored, n (%)	90 (98.9)	172 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.299 (1.069)
95% CI		(0.406, 26.839)
Log-rank p-value		0.242

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.5, 100.0)	95.9 (92.9, 98.9)
6 months	98.8 (96.5, 100.0)	95.9 (92.9, 98.9)
9 months	NE (NE, NE)	95.9 (92.9, 98.9)
12 months	NE (NE, NE)	95.9 (92.9, 98.9)
18 months	NE (NE, NE)	95.9 (92.9, 98.9)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	25 (27.5)	69 (38.5)
Number of Subjects Censored, n (%)	66 (72.5)	110 (61.5)
Time to first TEAE (months)		
25% percentile (95% CI)	1.87 (0.49, NE)	0.69 (0.69, 1.61)
Median (95% CI)	NE (NE, NE)	NE (6.41, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.463 (0.244)
95% CI		(0.907, 2.361)
Log-rank p-value		0.134

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	70.5 (60.6, 80.5)	63.5 (56.4, 70.7)
6 months	70.5 (60.6, 80.5)	59.1 (51.2, 67.0)
9 months	NE (NE, NE)	57.2 (48.7, 65.7)
12 months	NE (NE, NE)	57.2 (48.7, 65.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.91	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	4 (4.4)	27 (15.1)
Number of Subjects Censored, n (%)	87 (95.6)	152 (84.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.629 (0.539)
95% CI		(1.262, 10.439)
Log-rank p-value		0.011

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dysphonia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.1 (90.4, 99.8)	85.3 (80.1, 90.5)
6 months	95.1 (90.4, 99.8)	84.4 (78.9, 89.8)
9 months	NE (NE, NE)	84.4 (78.9, 89.8)
12 months	NE (NE, NE)	84.4 (78.9, 89.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	10 (11.0)	15 (8.4)
Number of Subjects Censored, n (%)	81 (89.0)	164 (91.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.654 (0.457)
95% CI		(0.267, 1.603)
Log-rank p-value		0.314

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Dyspnoea**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	88.5 (81.8, 95.3)	93.1 (89.3, 96.9)
6 months	88.5 (81.8, 95.3)	90.7 (85.8, 95.6)
9 months	NE (NE, NE)	88.7 (82.5, 94.9)
12 months	NE (NE, NE)	88.7 (82.5, 94.9)
18 months	NE (NE, NE)	88.7 (82.5, 94.9)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	14 (15.4)	15 (8.4)
Number of Subjects Censored, n (%)	77 (84.6)	164 (91.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.40, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.476 (0.390)
95% CI		(0.222, 1.021)
Log-rank p-value		0.056

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Cough**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.8 (74.3, 91.2)	91.9 (87.9, 96.0)
6 months	82.8 (74.3, 91.2)	91.0 (86.6, 95.4)
9 months	NE (NE, NE)	91.0 (86.6, 95.4)
12 months	NE (NE, NE)	91.0 (86.6, 95.4)
18 months	NE (NE, NE)	91.0 (86.6, 95.4)
Median Follow-up Time (months)	2.20	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	10 (5.6)
Number of Subjects Censored, n (%)	91 (100.0)	169 (94.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.034

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Epistaxis**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	94.1 (90.5, 97.6)
6 months	100.0 (100.0, 100.0)	94.1 (90.5, 97.6)
9 months	NE (NE, NE)	94.1 (90.5, 97.6)
12 months	NE (NE, NE)	94.1 (90.5, 97.6)
18 months	NE (NE, NE)	94.1 (90.5, 97.6)
Median Follow-up Time (months)	2.79	3.78

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	3 (1.7)
Number of Subjects Censored, n (%)	91 (100.0)	176 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.316

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Respiratory, thoracic and mediastinal disorders** and Preferred Term **Oropharyngeal pain**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.9 (97.3, 100.0)
6 months	100.0 (100.0, 100.0)	98.9 (97.3, 100.0)
9 months	NE (NE, NE)	95.7 (89.4, 100.0)
12 months	NE (NE, NE)	95.7 (89.4, 100.0)
18 months	NE (NE, NE)	95.7 (89.4, 100.0)
Median Follow-up Time (months)	2.79	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Vascular disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	16 (17.6)	71 (39.7)
Number of Subjects Censored, n (%)	75 (82.4)	108 (60.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.81, NE)	1.15 (0.69, 1.68)
Median (95% CI)	NE (NE, NE)	NE (4.60, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.227 (0.278)
95% CI		(1.291, 3.842)
Log-rank p-value		0.003

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Vascular disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.3 (72.7, 90.0)	60.4 (53.0, 67.7)
6 months	75.1 (60.8, 89.3)	56.0 (47.6, 64.4)
9 months	NE (NE, NE)	56.0 (47.6, 64.4)
12 months	NE (NE, NE)	56.0 (47.6, 64.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.27	2.76

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	8 (8.8)	64 (35.8)
Number of Subjects Censored, n (%)	83 (91.2)	115 (64.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.58 (0.69, 1.94)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.188 (0.376)
95% CI		(2.004, 8.749)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Vascular disorders** and Preferred Term **Hypertension**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.7 (82.9, 96.6)	63.2 (55.9, 70.5)
6 months	89.7 (82.9, 96.6)	62.0 (54.5, 69.6)
9 months	NE (NE, NE)	62.0 (54.5, 69.6)
12 months	NE (NE, NE)	62.0 (54.5, 69.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.56	2.79

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	11 (12.1)	66 (36.9)
Number of Subjects Censored, n (%)	80 (87.9)	113 (63.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	1.61 (0.72, 1.84)
Median (95% CI)	NE (NE, NE)	NE (7.20, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.878 (0.328)
95% CI		(1.514, 5.469)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.5 (80.5, 94.4)	63.9 (56.7, 71.1)
6 months	87.5 (80.5, 94.4)	62.0 (54.5, 69.5)
9 months	NE (NE, NE)	58.9 (49.6, 68.1)
12 months	NE (NE, NE)	50.5 (33.3, 67.7)
18 months	NE (NE, NE)	50.5 (33.3, 67.7)
Median Follow-up Time (months)	2.33	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	6 (6.6)	20 (11.2)
Number of Subjects Censored, n (%)	85 (93.4)	159 (88.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.264 (0.473)
95% CI		(0.500, 3.196)
Log-rank p-value		0.492

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Back pain**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.2 (87.9, 98.5)	90.4 (85.9, 94.9)
6 months	93.2 (87.9, 98.5)	87.0 (81.1, 92.8)
9 months	NE (NE, NE)	85.1 (78.3, 91.9)
12 months	NE (NE, NE)	85.1 (78.3, 91.9)
18 months	NE (NE, NE)	85.1 (78.3, 91.9)
Median Follow-up Time (months)	2.73	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	22 (12.3)
Number of Subjects Censored, n (%)	90 (98.9)	157 (87.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.20, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		9.437 (1.026)
95% CI		(1.263, 70.515)
Log-rank p-value		0.007

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Arthralgia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.8 (96.6, 100.0)	88.9 (84.2, 93.6)
6 months	98.8 (96.6, 100.0)	86.2 (80.3, 92.2)
9 months	NE (NE, NE)	82.6 (73.7, 91.6)
12 months	NE (NE, NE)	82.6 (73.7, 91.6)
18 months	NE (NE, NE)	82.6 (73.7, 91.6)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	12 (6.7)
Number of Subjects Censored, n (%)	91 (100.0)	167 (93.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.029

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Pain in extremity**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	93.1 (89.3, 96.9)
6 months	100.0 (100.0, 100.0)	93.1 (89.3, 96.9)
9 months	NE (NE, NE)	93.1 (89.3, 96.9)
12 months	NE (NE, NE)	93.1 (89.3, 96.9)
18 months	NE (NE, NE)	93.1 (89.3, 96.9)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	2 (2.2)	9 (5.0)
Number of Subjects Censored, n (%)	89 (97.8)	170 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.186 (0.783)
95% CI		(0.472, 10.136)
Log-rank p-value		0.309

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Myalgia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (94.6, 100.0)	94.7 (91.4, 98.1)
6 months	97.7 (94.6, 100.0)	94.7 (91.4, 98.1)
9 months	NE (NE, NE)	94.7 (91.4, 98.1)
12 months	NE (NE, NE)	94.7 (91.4, 98.1)
18 months	NE (NE, NE)	94.7 (91.4, 98.1)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	2 (1.1)
Number of Subjects Censored, n (%)	91 (100.0)	177 (98.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (7.52, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.463

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Musculoskeletal chest pain**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	99.4 (98.3, 100.0)
6 months	100.0 (100.0, 100.0)	99.4 (98.3, 100.0)
9 months	NE (NE, NE)	95.1 (86.8, 100.0)
12 months	NE (NE, NE)	95.1 (86.8, 100.0)
18 months	NE (NE, NE)	95.1 (86.8, 100.0)
Median Follow-up Time (months)	2.79	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	5 (2.8)
Number of Subjects Censored, n (%)	91 (100.0)	174 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.149

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Musculoskeletal and connective tissue disorders** and Preferred Term **Muscle spasms**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	96.9 (94.2, 99.6)
6 months	100.0 (100.0, 100.0)	96.9 (94.2, 99.6)
9 months	NE (NE, NE)	96.9 (94.2, 99.6)
12 months	NE (NE, NE)	96.9 (94.2, 99.6)
18 months	NE (NE, NE)	96.9 (94.2, 99.6)
Median Follow-up Time (months)	2.79	3.98

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	9 (9.9)	76 (42.5)
Number of Subjects Censored, n (%)	82 (90.1)	103 (57.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	0.76 (0.53, 1.61)
Median (95% CI)	NE (NE, NE)	6.24 (3.65, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.315 (0.354)
95% CI		(2.157, 8.632)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.7 (83.4, 96.1)	59.7 (52.2, 67.2)
6 months	89.7 (83.4, 96.1)	52.6 (44.1, 61.2)
9 months	NE (NE, NE)	49.7 (39.9, 59.5)
12 months	NE (NE, NE)	49.7 (39.9, 59.5)
18 months	NE (NE, NE)	49.7 (39.9, 59.5)
Median Follow-up Time (months)	2.73	2.46

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	6 (6.6)	50 (27.9)
Number of Subjects Censored, n (%)	85 (93.4)	129 (72.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	2.30 (1.38, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.111 (0.433)
95% CI		(1.758, 9.614)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Palmar-plantar erythrodysaesthesia syndrome**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.1 (87.7, 98.4)	73.4 (66.8, 80.1)
6 months	93.1 (87.7, 98.4)	69.1 (61.6, 76.6)
9 months	NE (NE, NE)	69.1 (61.6, 76.6)
12 months	NE (NE, NE)	69.1 (61.6, 76.6)
18 months	NE (NE, NE)	69.1 (61.6, 76.6)
Median Follow-up Time (months)	2.79	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	4 (4.4)	9 (5.0)
Number of Subjects Censored, n (%)	87 (95.6)	170 (95.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.037 (0.604)
95% CI		(0.317, 3.387)
Log-rank p-value		0.970

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Rash**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (91.2, 99.8)	94.5 (91.0, 98.0)
6 months	95.5 (91.2, 99.8)	94.5 (91.0, 98.0)
9 months	NE (NE, NE)	94.5 (91.0, 98.0)
12 months	NE (NE, NE)	94.5 (91.0, 98.0)
18 months	NE (NE, NE)	94.5 (91.0, 98.0)
Median Follow-up Time (months)	2.79	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	6 (3.4)
Number of Subjects Censored, n (%)	91 (100.0)	173 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.122

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Skin and subcutaneous tissue disorders** and Preferred Term **Dry skin**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.0 (94.4, 99.6)
6 months	100.0 (100.0, 100.0)	96.0 (92.8, 99.2)
9 months	NE (NE, NE)	96.0 (92.8, 99.2)
12 months	NE (NE, NE)	96.0 (92.8, 99.2)
18 months	NE (NE, NE)	96.0 (92.8, 99.2)
Median Follow-up Time (months)	2.79	3.98

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	15 (16.5)	47 (26.3)
Number of Subjects Censored, n (%)	76 (83.5)	132 (73.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.81, NE)	4.57 (1.61, NE)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.0, 6.8*	0.0, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.301 (0.303)
95% CI		(0.719, 2.356)
Log-rank p-value		0.406

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	81.2 (72.4, 89.9)	76.5 (70.0, 82.9)
6 months	81.2 (72.4, 89.9)	69.0 (60.4, 77.7)
9 months	NE (NE, NE)	66.8 (57.4, 76.2)
12 months	NE (NE, NE)	66.8 (57.4, 76.2)
18 months	NE (NE, NE)	66.8 (57.4, 76.2)
Median Follow-up Time (months)	2.33	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	3 (3.3)	19 (10.6)
Number of Subjects Censored, n (%)	88 (96.7)	160 (89.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Median (95% CI)	NE (NE, NE)	18.04 (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	18.04 (NE, NE)
Min, Max	0.4*, 8.4*	0.0, 18.0
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.606 (0.628)
95% CI		(0.761, 8.925)
Log-rank p-value		0.105

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Headache**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.5 (90.5, 100.0)	91.4 (87.3, 95.6)
6 months	95.5 (90.5, 100.0)	88.9 (83.6, 94.2)
9 months	NE (NE, NE)	86.7 (80.1, 93.4)
12 months	NE (NE, NE)	86.7 (80.1, 93.4)
18 months	NE (NE, NE)	86.7 (80.1, 93.4)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	3 (3.3)	4 (2.2)
Number of Subjects Censored, n (%)	88 (96.7)	175 (97.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.626 (0.764)
95% CI		(0.140, 2.802)
Log-rank p-value		0.526

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dysgeusia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.5 (92.7, 100.0)	97.7 (95.5, 99.9)
6 months	96.5 (92.7, 100.0)	97.7 (95.5, 99.9)
9 months	NE (NE, NE)	97.7 (95.5, 99.9)
12 months	NE (NE, NE)	97.7 (95.5, 99.9)
18 months	NE (NE, NE)	97.7 (95.5, 99.9)
Median Follow-up Time (months)	2.79	3.98

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	5 (2.8)
Number of Subjects Censored, n (%)	91 (100.0)	174 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.130

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Nervous system disorders** and Preferred Term **Dizziness**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.1 (94.7, 99.6)
6 months	100.0 (100.0, 100.0)	97.1 (94.7, 99.6)
9 months	NE (NE, NE)	97.1 (94.7, 99.6)
12 months	NE (NE, NE)	97.1 (94.7, 99.6)
18 months	NE (NE, NE)	97.1 (94.7, 99.6)
Median Follow-up Time (months)	2.79	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	12 (13.2)	46 (25.7)
Number of Subjects Censored, n (%)	79 (86.8)	133 (74.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.71, NE)	3.91 (2.04, 11.96)
Median (95% CI)	NE (NE, NE)	11.96 (11.96, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (11.96, NE)
Min, Max	0.2, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.396 (0.332)
95% CI		(0.728, 2.678)
Log-rank p-value		0.366

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Renal and urinary disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.0 (79.7, 94.2)	78.1 (71.9, 84.4)
6 months	78.3 (60.8, 95.7)	69.2 (60.5, 77.8)
9 months	NE (NE, NE)	66.3 (56.3, 76.3)
12 months	NE (NE, NE)	44.2 (8.2, 80.2)
18 months	NE (NE, NE)	44.2 (8.2, 80.2)
Median Follow-up Time (months)	2.46	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	6 (6.6)	35 (19.6)
Number of Subjects Censored, n (%)	85 (93.4)	144 (80.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	8.38 (3.35, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.142 (0.449)
95% CI		(0.888, 5.169)
Log-rank p-value		0.104

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Proteinuria**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	93.0 (87.6, 98.4)	82.6 (76.8, 88.4)
6 months	93.0 (87.6, 98.4)	76.4 (68.7, 84.2)
9 months	NE (NE, NE)	71.0 (58.4, 83.5)
12 months	NE (NE, NE)	71.0 (58.4, 83.5)
18 months	NE (NE, NE)	71.0 (58.4, 83.5)
Median Follow-up Time (months)	2.60	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	2 (2.2)	3 (1.7)
Number of Subjects Censored, n (%)	89 (97.8)	176 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 8.4*	0.4, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.599 (0.933)
95% CI		(0.096, 3.726)
Log-rank p-value		0.500

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Renal and urinary disorders** and Preferred Term **Haematuria**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (94.6, 100.0)	98.9 (97.3, 100.0)
6 months	97.7 (94.6, 100.0)	97.8 (95.3, 100.0)
9 months	NE (NE, NE)	97.8 (95.3, 100.0)
12 months	NE (NE, NE)	97.8 (95.3, 100.0)
18 months	NE (NE, NE)	97.8 (95.3, 100.0)
Median Follow-up Time (months)	2.79	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	10 (11.0)	32 (17.9)
Number of Subjects Censored, n (%)	81 (89.0)	147 (82.1)
Time to first TEAE (months)		
25% percentile (95% CI)	5.78 (5.78, NE)	8.21 (5.09, NE)
Median (95% CI)	NE (5.78, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (5.78, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.090 (0.376)
95% CI		(0.522, 2.277)
Log-rank p-value		0.811

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.0 (82.2, 95.8)	86.4 (81.1, 91.6)
6 months	59.4 (11.6, 100.0)	75.2 (66.3, 84.0)
9 months	NE (NE, NE)	70.2 (57.6, 82.7)
12 months	NE (NE, NE)	70.2 (57.6, 82.7)
18 months	NE (NE, NE)	70.2 (57.6, 82.7)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	6 (3.4)
Number of Subjects Censored, n (%)	90 (98.9)	173 (96.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (4.34, NE)	NE (NE, NE)
Median (95% CI)	NE (4.34, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.2, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.670 (1.129)
95% CI		(0.183, 15.264)
Log-rank p-value		0.665

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Urinary tract infection**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.1 (94.6, 99.6)
6 months	90.0 (71.4, 100.0)	95.2 (90.9, 99.6)
9 months	NE (NE, NE)	95.2 (90.9, 99.6)
12 months	NE (NE, NE)	95.2 (90.9, 99.6)
18 months	NE (NE, NE)	95.2 (90.9, 99.6)
Median Follow-up Time (months)	2.79	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	2 (2.2)	3 (1.7)
Number of Subjects Censored, n (%)	89 (97.8)	176 (98.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.512 (0.954)
95% CI		(0.079, 3.323)
Log-rank p-value		0.444

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **COVID-19**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.5 (94.2, 100.0)	98.8 (97.0, 100.0)
6 months	97.5 (94.2, 100.0)	97.3 (94.0, 100.0)
9 months	NE (NE, NE)	97.3 (94.0, 100.0)
12 months	NE (NE, NE)	97.3 (94.0, 100.0)
18 months	NE (NE, NE)	97.3 (94.0, 100.0)
Median Follow-up Time (months)	2.79	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	7 (3.9)
Number of Subjects Censored, n (%)	90 (98.9)	172 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.5, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.358 (1.084)
95% CI		(0.281, 19.750)
Log-rank p-value		0.412

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Infections and infestations** and Preferred Term **Pneumonia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.9 (96.7, 100.0)	95.6 (92.3, 98.8)
6 months	98.9 (96.7, 100.0)	95.6 (92.3, 98.8)
9 months	NE (NE, NE)	95.6 (92.3, 98.8)
12 months	NE (NE, NE)	95.6 (92.3, 98.8)
18 months	NE (NE, NE)	95.6 (92.3, 98.8)
Median Follow-up Time (months)	2.79	4.04

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	13 (14.3)	24 (13.4)
Number of Subjects Censored, n (%)	78 (85.7)	155 (86.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (2.79, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.3, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.678 (0.354)
95% CI		(0.339, 1.357)
Log-rank p-value		0.272

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.9 (75.6, 92.1)	87.5 (82.4, 92.5)
6 months	83.9 (75.6, 92.1)	83.9 (77.7, 90.2)
9 months	NE (NE, NE)	83.9 (77.7, 90.2)
12 months	NE (NE, NE)	83.9 (77.7, 90.2)
18 months	NE (NE, NE)	83.9 (77.7, 90.2)
Median Follow-up Time (months)	2.56	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	11 (12.1)	13 (7.3)
Number of Subjects Censored, n (%)	80 (87.9)	166 (92.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.412 (0.425)
95% CI		(0.179, 0.948)
Log-rank p-value		0.034

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Anaemia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.7 (77.6, 93.8)	93.3 (89.5, 97.2)
6 months	85.7 (77.6, 93.8)	91.0 (86.1, 95.9)
9 months	NE (NE, NE)	91.0 (86.1, 95.9)
12 months	NE (NE, NE)	91.0 (86.1, 95.9)
18 months	NE (NE, NE)	91.0 (86.1, 95.9)
Median Follow-up Time (months)	2.56	3.94

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	1 (1.1)	7 (3.9)
Number of Subjects Censored, n (%)	90 (98.9)	172 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.687 (1.081)
95% CI		(0.323, 22.379)
Log-rank p-value		0.351

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Blood and lymphatic system disorders** and Preferred Term **Thrombocytopenia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.6 (96.0, 100.0)	95.8 (92.7, 98.9)
6 months	98.6 (96.0, 100.0)	95.8 (92.7, 98.9)
9 months	NE (NE, NE)	95.8 (92.7, 98.9)
12 months	NE (NE, NE)	95.8 (92.7, 98.9)
18 months	NE (NE, NE)	95.8 (92.7, 98.9)
Median Follow-up Time (months)	2.79	3.98

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Endocrine disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	41 (22.9)
Number of Subjects Censored, n (%)	91 (100.0)	138 (77.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	4.60 (2.79, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Endocrine disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	81.4 (75.5, 87.4)
6 months	100.0 (100.0, 100.0)	67.7 (58.0, 77.3)
9 months	NE (NE, NE)	67.7 (58.0, 77.3)
12 months	NE (NE, NE)	67.7 (58.0, 77.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.02

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	39 (21.8)
Number of Subjects Censored, n (%)	91 (100.0)	140 (78.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.52 (3.58, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 12.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Endocrine disorders** and Preferred Term **Hypothyroidism**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	82.7 (77.0, 88.5)
6 months	100.0 (100.0, 100.0)	70.6 (61.4, 79.8)
9 months	NE (NE, NE)	66.2 (54.1, 78.2)
12 months	NE (NE, NE)	66.2 (54.1, 78.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	3 (3.3)	26 (14.5)
Number of Subjects Censored, n (%)	88 (96.7)	153 (85.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (5.29, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.194 (0.615)
95% CI		(0.957, 10.657)
Log-rank p-value		0.042

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.3 (92.2, 100.0)	87.3 (82.2, 92.4)
6 months	96.3 (92.2, 100.0)	80.9 (73.5, 88.2)
9 months	NE (NE, NE)	80.9 (73.5, 88.2)
12 months	NE (NE, NE)	80.9 (73.5, 88.2)
18 months	NE (NE, NE)	80.9 (73.5, 88.2)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	3 (3.3)	12 (6.7)
Number of Subjects Censored, n (%)	88 (96.7)	167 (93.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.0, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.599 (0.649)
95% CI		(0.448, 5.703)
Log-rank p-value		0.438

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Insomnia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.3 (92.2, 100.0)	93.2 (89.2, 97.1)
6 months	96.3 (92.2, 100.0)	92.2 (87.9, 96.5)
9 months	NE (NE, NE)	92.2 (87.9, 96.5)
12 months	NE (NE, NE)	92.2 (87.9, 96.5)
18 months	NE (NE, NE)	92.2 (87.9, 96.5)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	4 (2.2)
Number of Subjects Censored, n (%)	91 (100.0)	175 (97.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.326

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Anxiety**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	98.2 (96.3, 100.0)
6 months	100.0 (100.0, 100.0)	96.8 (93.5, 100.0)
9 months	NE (NE, NE)	96.8 (93.5, 100.0)
12 months	NE (NE, NE)	96.8 (93.5, 100.0)
18 months	NE (NE, NE)	96.8 (93.5, 100.0)
Median Follow-up Time (months)	2.79	4.17

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	0	5 (2.8)
Number of Subjects Censored, n (%)	91 (100.0)	174 (97.2)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.265

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Psychiatric disorders** and Preferred Term **Confusional state**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.5 (95.1, 99.9)
6 months	100.0 (100.0, 100.0)	96.0 (92.2, 99.8)
9 months	NE (NE, NE)	96.0 (92.2, 99.8)
12 months	NE (NE, NE)	96.0 (92.2, 99.8)
18 months	NE (NE, NE)	96.0 (92.2, 99.8)
Median Follow-up Time (months)	2.79	4.37

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	12 (13.2)	21 (11.7)
Number of Subjects Censored, n (%)	79 (86.8)	158 (88.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.717 (0.365)
95% CI		(0.350, 1.467)
Log-rank p-value		0.357

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Hepatobiliary disorders**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	85.6 (78.0, 93.2)	88.5 (83.6, 93.4)
6 months	85.6 (78.0, 93.2)	86.0 (80.2, 91.9)
9 months	NE (NE, NE)	86.0 (80.2, 91.9)
12 months	NE (NE, NE)	86.0 (80.2, 91.9)
18 months	NE (NE, NE)	86.0 (80.2, 91.9)
Median Follow-up Time (months)	2.79	3.75

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	2 (2.2)	10 (5.6)
Number of Subjects Censored, n (%)	89 (97.8)	169 (94.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.6*, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.978 (0.780)
95% CI		(0.429, 9.119)
Log-rank p-value		0.382

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hypertransaminasaemia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (93.4, 100.0)	94.4 (90.9, 98.0)
6 months	97.2 (93.4, 100.0)	92.9 (88.2, 97.5)
9 months	NE (NE, NE)	92.9 (88.2, 97.5)
12 months	NE (NE, NE)	92.9 (88.2, 97.5)
18 months	NE (NE, NE)	92.9 (88.2, 97.5)
Median Follow-up Time (months)	2.79	3.98

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3N
Summary of Time to Onset of TEAE by SOC/PT by Prior TAS-102 and/or Regorafenib
Safety Population
TEAE in SOC Term **Hepatobiliary disorders** and Preferred Term **Hyperbilirubinaemia**
TAS-102 and Regorafenib

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Number of Subjects with Events, n (%)	2 (2.2)	7 (3.9)
Number of Subjects Censored, n (%)	89 (97.8)	172 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 8.4*	0.1, 18.6*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.389 (0.809)
95% CI		(0.285, 6.782)
Log-rank p-value		0.676

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=91	Fruquintinib + BSC N=179
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (94.6, 100.0)	96.3 (93.4, 99.2)
6 months	97.7 (94.6, 100.0)	95.3 (91.8, 98.8)
9 months	NE (NE, NE)	95.3 (91.8, 98.8)
12 months	NE (NE, NE)	95.3 (91.8, 98.8)
18 months	NE (NE, NE)	95.3 (91.8, 98.8)
Median Follow-up Time (months)	2.79	3.98

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	93 (60.0)	232 (69.3)
Number of Subjects Censored, n (%)	62 (40.0)	103 (30.7)
Time to first TEAE (months)		
25% percentile (95% CI)	0.69 (0.46, 0.72)	0.36 (0.26, 0.59)
Median (95% CI)	1.61 (1.15, 2.50)	1.12 (0.92, 1.61)
75% percentile (95% CI)	NE (4.70, NE)	6.47 (3.91, NE)

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Min, Max	0.0, 6.5*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.159 (0.125)
95% CI		(0.908, 1.480)
Log-rank p-value		0.296

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	38.5 (30.3, 46.6)	36.9 (31.6, 42.2)
6 months	26.6 (10.0, 43.3)	25.0 (19.4, 30.7)
9 months	NE (NE, NE)	20.1 (13.2, 27.0)
12 months	NE (NE, NE)	20.1 (13.2, 27.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.38	1.08

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	38 (24.5)	116 (34.6)
Number of Subjects Censored, n (%)	117 (75.5)	219 (65.4)
Time to first TEAE (months)		
25% percentile (95% CI)	2.76 (0.95, NE)	1.18 (0.92, 2.43)
Median (95% CI)	NE (4.70, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.324 (0.189)
95% CI		(0.915, 1.917)
Log-rank p-value		0.137

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Asthenia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	74.1 (66.7, 81.5)	67.2 (62.1, 72.4)
6 months	63.6 (43.3, 83.8)	63.0 (57.3, 68.6)
9 months	NE (NE, NE)	59.1 (51.5, 66.8)
12 months	NE (NE, NE)	59.1 (51.5, 66.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.23	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	26 (16.8)	69 (20.6)
Number of Subjects Censored, n (%)	129 (83.2)	266 (79.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (3.65, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.116 (0.234)
95% CI		(0.706, 1.764)
Log-rank p-value		0.646

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Fatigue**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.3 (76.1, 88.5)	80.8 (76.5, 85.1)
6 months	82.3 (76.1, 88.5)	76.2 (70.9, 81.5)
9 months	NE (NE, NE)	76.2 (70.9, 81.5)
12 months	NE (NE, NE)	76.2 (70.9, 81.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.27	2.86

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	18 (11.6)	36 (10.7)
Number of Subjects Censored, n (%)	137 (88.4)	299 (89.3)
Time to first TEAE (months)		
25% percentile (95% CI)	4.70 (4.70, NE)	NE (NE, NE)
Median (95% CI)	NE (4.70, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.5*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.812 (0.296)
95% CI		(0.455, 1.449)
Log-rank p-value		0.451

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Pyrexia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.9 (80.8, 92.9)	90.4 (87.2, 93.6)
6 months	74.5 (51.3, 97.6)	87.6 (83.5, 91.8)
9 months	NE (NE, NE)	86.4 (81.7, 91.1)
12 months	NE (NE, NE)	86.4 (81.7, 91.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.46	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	4 (2.6)	41 (12.2)
Number of Subjects Censored, n (%)	151 (97.4)	294 (87.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.1, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.335 (0.526)
95% CI		(1.546, 12.161)
Log-rank p-value		0.002

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Mucosal inflammation**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (94.5, 99.9)	88.9 (85.5, 92.4)
6 months	97.2 (94.5, 99.9)	87.2 (83.4, 91.1)
9 months	NE (NE, NE)	83.6 (77.3, 89.8)
12 months	NE (NE, NE)	83.6 (77.3, 89.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.63	3.22

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	25 (16.1)	23 (6.9)
Number of Subjects Censored, n (%)	130 (83.9)	312 (93.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.19, NE)	NE (12.22, NE)
Median (95% CI)	NE (NE, NE)	NE (12.22, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.262 (0.307)
95% CI		(0.144, 0.478)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Disease progression**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	82.8 (76.3, 89.4)	95.2 (92.9, 97.6)
6 months	75.3 (63.6, 87.1)	90.7 (86.5, 94.8)
9 months	NE (NE, NE)	90.7 (86.5, 94.8)
12 months	NE (NE, NE)	90.7 (86.5, 94.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	14 (9.0)	17 (5.1)
Number of Subjects Censored, n (%)	141 (91.0)	318 (94.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.2, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.479 (0.368)
95% CI		(0.233, 0.985)
Log-rank p-value		0.039

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Oedema peripheral**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	90.1 (85.1, 95.2)	95.0 (92.6, 97.4)
6 months	90.1 (85.1, 95.2)	95.0 (92.6, 97.4)
9 months	NE (NE, NE)	91.6 (84.7, 98.5)
12 months	NE (NE, NE)	91.6 (84.7, 98.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.63	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	5 (3.2)	13 (3.9)
Number of Subjects Censored, n (%)	150 (96.8)	322 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (9.72, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.623 (0.575)
95% CI		(0.202, 1.922)
Log-rank p-value		0.408

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **General physical health deterioration**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.5 (93.4, 99.6)	97.8 (96.2, 99.4)
6 months	96.5 (93.4, 99.6)	96.5 (94.0, 98.9)
9 months	NE (NE, NE)	94.4 (89.8, 99.1)
12 months	NE (NE, NE)	82.1 (68.4, 95.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	4 (2.6)	8 (2.4)
Number of Subjects Censored, n (%)	151 (97.4)	327 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.4, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.637 (0.642)
95% CI		(0.181, 2.240)
Log-rank p-value		0.426

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Condition aggravated**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	96.5 (92.8, 100.0)	98.0 (96.4, 99.6)
6 months	96.5 (92.8, 100.0)	97.3 (95.3, 99.4)
9 months	NE (NE, NE)	95.2 (90.6, 99.8)
12 months	NE (NE, NE)	95.2 (90.6, 99.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	2 (1.3)	9 (2.7)
Number of Subjects Censored, n (%)	153 (98.7)	326 (97.3)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.843 (0.797)
95% CI		(0.387, 8.780)
Log-rank p-value		0.436

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **General disorders and administration site conditions** and Preferred Term **Chills**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.9, 100.0)	97.9 (96.4, 99.4)
6 months	98.7 (96.9, 100.0)	97.3 (95.4, 99.2)
9 months	NE (NE, NE)	94.4 (88.4, 100.0)
12 months	NE (NE, NE)	94.4 (88.4, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	96 (61.9)	224 (66.9)
Number of Subjects Censored, n (%)	59 (38.1)	111 (33.1)
Time to first TEAE (months)		
25% percentile (95% CI)	0.43 (0.26, 0.62)	0.49 (0.36, 0.69)
Median (95% CI)	1.31 (0.72, 1.61)	1.58 (0.95, 2.04)
75% percentile (95% CI)	4.34 (2.92, NE)	5.95 (4.70, 7.79)
Min, Max	0.0, 5.0*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.866 (0.125)
95% CI		(0.677, 1.107)
Log-rank p-value		0.270

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	33.9 (24.7, 43.0)	39.5 (34.1, 44.9)
6 months	NE (NE, NE)	24.9 (18.6, 31.3)
9 months	NE (NE, NE)	15.3 (7.5, 23.1)
12 months	NE (NE, NE)	12.2 (4.0, 20.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	1.02	1.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	16 (10.3)	81 (24.2)
Number of Subjects Censored, n (%)	139 (89.7)	254 (75.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	5.39 (2.37, 7.33)
Median (95% CI)	NE (NE, NE)	NE (10.87, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.053 (0.277)
95% CI		(1.193, 3.532)
Log-rank p-value		0.008

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Diarrhoea**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	89.3 (84.4, 94.3)	78.9 (74.4, 83.4)
6 months	89.3 (84.4, 94.3)	72.1 (66.0, 78.1)
9 months	NE (NE, NE)	67.4 (59.8, 75.1)
12 months	NE (NE, NE)	59.9 (44.5, 75.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.46	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	32 (20.6)	57 (17.0)
Number of Subjects Censored, n (%)	123 (79.4)	278 (83.0)
Time to first TEAE (months)		
25% percentile (95% CI)	4.34 (1.61, NE)	9.20 (5.55, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.582 (0.230)
95% CI		(0.371, 0.914)
Log-rank p-value		0.019

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Nausea**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	79.1 (72.5, 85.7)	84.5 (80.4, 88.6)
6 months	71.2 (55.3, 87.1)	80.4 (75.3, 85.5)
9 months	NE (NE, NE)	78.4 (72.0, 84.7)
12 months	NE (NE, NE)	71.8 (61.3, 82.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.27	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	30 (19.4)	58 (17.3)
Number of Subjects Censored, n (%)	125 (80.6)	277 (82.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (1.61, NE)	9.23 (6.18, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.641 (0.235)
95% CI		(0.404, 1.015)
Log-rank p-value		0.074

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	77.3 (69.1, 85.5)	84.9 (80.9, 88.9)
6 months	77.3 (69.1, 85.5)	81.8 (77.0, 86.5)
9 months	NE (NE, NE)	76.2 (69.2, 83.3)
12 months	NE (NE, NE)	67.6 (54.4, 80.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.27	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	17 (11.0)	57 (17.0)
Number of Subjects Censored, n (%)	138 (89.0)	278 (83.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.15, NE)	9.33 (5.62, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.171 (0.283)
95% CI		(0.672, 2.039)
Log-rank p-value		0.558

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Constipation**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	86.8 (79.3, 94.3)	85.5 (81.5, 89.5)
6 months	83.5 (74.0, 93.0)	79.1 (73.5, 84.7)
9 months	NE (NE, NE)	75.9 (68.9, 82.8)
12 months	NE (NE, NE)	72.3 (62.7, 81.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.46	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	25 (16.1)	47 (14.0)
Number of Subjects Censored, n (%)	130 (83.9)	288 (86.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.52, NE)	NE (7.10, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.1, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.637 (0.257)
95% CI		(0.384, 1.054)
Log-rank p-value		0.086

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Vomiting**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	83.0 (76.7, 89.3)	89.2 (85.7, 92.6)
6 months	78.9 (68.9, 88.8)	83.0 (77.8, 88.1)
9 months	NE (NE, NE)	80.2 (73.9, 86.4)
12 months	NE (NE, NE)	76.8 (68.0, 85.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.40	3.25

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	4 (2.6)	51 (15.2)
Number of Subjects Censored, n (%)	151 (97.4)	284 (84.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		5.683 (0.521)
95% CI		(2.047, 15.777)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Stomatitis**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.3 (94.6, 99.9)	85.9 (82.1, 89.7)
6 months	97.3 (94.6, 99.9)	83.4 (79.0, 87.8)
9 months	NE (NE, NE)	81.8 (76.4, 87.1)
12 months	NE (NE, NE)	81.8 (76.4, 87.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.73	3.06

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	6 (3.9)	30 (9.0)
Number of Subjects Censored, n (%)	149 (96.1)	305 (91.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.836 (0.455)
95% CI		(0.752, 4.482)
Log-rank p-value		0.176

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Abdominal pain upper**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.9 (92.7, 99.1)	92.9 (90.0, 95.7)
6 months	95.9 (92.7, 99.1)	88.7 (84.5, 93.0)
9 months	NE (NE, NE)	86.6 (80.7, 92.5)
12 months	NE (NE, NE)	86.6 (80.7, 92.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	3.35

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	3 (1.9)	11 (3.3)
Number of Subjects Censored, n (%)	152 (98.1)	324 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.363 (0.666)
95% CI		(0.369, 5.033)
Log-rank p-value		0.669

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Proctalgia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.8 (95.4, 100.0)	97.3 (95.5, 99.0)
6 months	97.8 (95.4, 100.0)	96.3 (93.7, 98.9)
9 months	NE (NE, NE)	94.3 (89.7, 98.9)
12 months	NE (NE, NE)	94.3 (89.7, 98.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	4 (2.6)	7 (2.1)
Number of Subjects Censored, n (%)	151 (97.4)	328 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.2, 6.8*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.633 (0.642)
95% CI		(0.180, 2.231)
Log-rank p-value		0.501

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dry mouth**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.0 (94.0, 99.9)	97.7 (96.0, 99.4)
6 months	97.0 (94.0, 99.9)	97.7 (96.0, 99.4)
9 months	NE (NE, NE)	97.7 (96.0, 99.4)
12 months	NE (NE, NE)	97.7 (96.0, 99.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.73	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	11 (7.1)	3 (0.9)
Number of Subjects Censored, n (%)	144 (92.9)	332 (99.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.084 (0.699)
95% CI		(0.021, 0.329)
Log-rank p-value		<.001

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Ascites**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.2 (87.7, 96.7)	99.4 (98.5, 100.0)
6 months	92.2 (87.7, 96.7)	98.3 (96.0, 100.0)
9 months	NE (NE, NE)	98.3 (96.0, 100.0)
12 months	NE (NE, NE)	98.3 (96.0, 100.0)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	0	10 (3.0)
Number of Subjects Censored, n (%)	155 (100.0)	325 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.038

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Gastrointestinal disorders** and Preferred Term **Dyspepsia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.1 (95.1, 99.0)
6 months	100.0 (100.0, 100.0)	97.1 (95.1, 99.0)
9 months	NE (NE, NE)	94.9 (90.3, 99.5)
12 months	NE (NE, NE)	94.9 (90.3, 99.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	46 (29.7)	145 (43.3)
Number of Subjects Censored, n (%)	109 (70.3)	190 (56.7)
Time to first TEAE (months)		
25% percentile (95% CI)	1.54 (0.76, 4.27)	1.31 (0.95, 1.61)
Median (95% CI)	NE (4.27, NE)	6.28 (3.94, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 12.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.272 (0.172)
95% CI		(0.909, 1.781)
Log-rank p-value		0.168

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	70.1 (62.6, 77.7)	59.4 (53.9, 64.9)
6 months	59.2 (43.0, 75.4)	51.8 (45.4, 58.1)
9 months	NE (NE, NE)	47.8 (40.4, 55.3)
12 months	NE (NE, NE)	44.2 (34.4, 53.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.17	2.73

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	30 (19.4)	94 (28.1)
Number of Subjects Censored, n (%)	125 (80.6)	241 (71.9)
Time to first TEAE (months)		
25% percentile (95% CI)	4.27 (1.84, NE)	2.73 (1.68, 3.94)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.300 (0.212)
95% CI		(0.857, 1.972)
Log-rank p-value		0.208

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Decreased appetite**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	80.3 (73.8, 86.8)	72.6 (67.6, 77.7)
6 months	73.0 (58.1, 87.8)	68.5 (62.8, 74.1)
9 months	NE (NE, NE)	68.5 (62.8, 74.1)
12 months	NE (NE, NE)	64.9 (56.2, 73.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.33	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	3 (1.9)	23 (6.9)
Number of Subjects Censored, n (%)	152 (98.1)	312 (93.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.657 (0.620)
95% CI		(0.787, 8.963)
Log-rank p-value		0.094

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypokalaemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.1 (95.9, 100.0)	93.3 (90.4, 96.2)
6 months	98.1 (95.9, 100.0)	92.0 (88.7, 95.4)
9 months	NE (NE, NE)	90.0 (85.0, 95.1)
12 months	NE (NE, NE)	90.0 (85.0, 95.1)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	3 (1.9)	13 (3.9)
Number of Subjects Censored, n (%)	152 (98.1)	322 (96.1)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.3, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.137 (0.669)
95% CI		(0.306, 4.221)
Log-rank p-value		0.782

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyponatraemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.9, 100.0)	97.4 (95.7, 99.2)
6 months	94.9 (87.4, 100.0)	94.4 (90.9, 97.8)
9 months	NE (NE, NE)	92.6 (87.7, 97.5)
12 months	NE (NE, NE)	92.6 (87.7, 97.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	2 (1.3)	11 (3.3)
Number of Subjects Censored, n (%)	153 (98.7)	324 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.128 (0.777)
95% CI		(0.465, 9.753)
Log-rank p-value		0.324

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperuricaemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.7 (96.9, 100.0)	96.7 (94.7, 98.7)
6 months	98.7 (96.9, 100.0)	96.2 (93.9, 98.4)
9 months	NE (NE, NE)	96.2 (93.9, 98.4)
12 months	NE (NE, NE)	96.2 (93.9, 98.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	3 (1.9)	8 (2.4)
Number of Subjects Censored, n (%)	152 (98.1)	327 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.5, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.938 (0.685)
95% CI		(0.245, 3.593)
Log-rank p-value		0.901

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypoalbuminaemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.0 (95.8, 100.0)	97.6 (95.9, 99.4)
6 months	98.0 (95.8, 100.0)	96.7 (94.2, 99.2)
9 months	NE (NE, NE)	96.7 (94.2, 99.2)
12 months	NE (NE, NE)	96.7 (94.2, 99.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	0	11 (3.3)
Number of Subjects Censored, n (%)	155 (100.0)	324 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		NE (NE)
95% CI		(NE, NE)
Log-rank p-value		0.044

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypomagnesaemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	100.0 (100.0, 100.0)	97.1 (95.3, 99.0)
6 months	100.0 (100.0, 100.0)	96.5 (94.4, 98.7)
9 months	NE (NE, NE)	94.7 (90.7, 98.8)
12 months	NE (NE, NE)	94.7 (90.7, 98.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	3 (1.9)	8 (2.4)
Number of Subjects Censored, n (%)	152 (98.1)	327 (97.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.988 (0.688)
95% CI		(0.257, 3.804)
Log-rank p-value		0.940

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Dehydration**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.2 (93.8, 100.0)	97.4 (95.5, 99.2)
6 months	97.2 (93.8, 100.0)	97.4 (95.5, 99.2)
9 months	NE (NE, NE)	97.4 (95.5, 99.2)
12 months	NE (NE, NE)	97.4 (95.5, 99.2)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	1 (0.6)	11 (3.3)
Number of Subjects Censored, n (%)	154 (99.4)	324 (96.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.634 (1.056)
95% CI		(0.459, 28.763)
Log-rank p-value		0.181

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hyperglycaemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (98.1, 100.0)	97.4 (95.7, 99.2)
6 months	99.3 (98.1, 100.0)	95.9 (93.1, 98.7)
9 months	NE (NE, NE)	94.8 (91.2, 98.3)
12 months	NE (NE, NE)	94.8 (91.2, 98.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	1 (0.6)	7 (2.1)
Number of Subjects Censored, n (%)	154 (99.4)	328 (97.9)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		3.026 (1.078)
95% CI		(0.366, 25.040)
Log-rank p-value		0.291

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypertriglyceridaemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (98.0, 100.0)	97.8 (96.1, 99.4)
6 months	99.3 (98.0, 100.0)	97.8 (96.1, 99.4)
9 months	NE (NE, NE)	97.8 (96.1, 99.4)
12 months	NE (NE, NE)	97.8 (96.1, 99.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	1 (0.6)	10 (3.0)
Number of Subjects Censored, n (%)	154 (99.4)	325 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 16.9*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.725 (1.082)
95% CI		(0.207, 14.394)
Log-rank p-value		0.613

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Metabolism and nutrition disorders** and Preferred Term **Hypophosphataemia**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.2 (97.7, 100.0)	98.5 (97.1, 100.0)
6 months	99.2 (97.7, 100.0)	93.9 (89.9, 97.9)
9 months	NE (NE, NE)	93.9 (89.9, 97.9)
12 months	NE (NE, NE)	93.9 (89.9, 97.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.71

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	48 (31.0)	141 (42.1)
Number of Subjects Censored, n (%)	107 (69.0)	194 (57.9)
Time to first TEAE (months)		
25% percentile (95% CI)	1.61 (0.92, 3.55)	1.45 (0.95, 1.61)
Median (95% CI)	5.82 (5.82, NE)	7.16 (5.49, NE)
75% percentile (95% CI)	NE (5.82, NE)	NE (NE, NE)
Min, Max	0.0, 6.5*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.193 (0.170)
95% CI		(0.855, 1.664)
Log-rank p-value		0.309

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	68.0 (60.1, 75.8)	60.4 (55.0, 65.9)
6 months	42.3 (7.6, 77.0)	53.4 (47.0, 59.8)
9 months	NE (NE, NE)	47.0 (39.1, 54.9)
12 months	NE (NE, NE)	47.0 (39.1, 54.9)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.23	2.83

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	15 (9.7)	46 (13.7)
Number of Subjects Censored, n (%)	140 (90.3)	289 (86.3)
Time to first TEAE (months)		
25% percentile (95% CI)	5.82 (5.82, NE)	NE (7.85, NE)
Median (95% CI)	NE (5.82, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (5.82, NE)	NE (NE, NE)
Min, Max	0.4*, 6.5*	0.0, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.095 (0.307)
95% CI		(0.600, 1.998)
Log-rank p-value		0.751

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Weight decreased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	87.7 (81.4, 94.0)	88.1 (84.5, 91.6)
6 months	58.5 (11.5, 100.0)	84.3 (79.6, 89.1)
9 months	NE (NE, NE)	79.9 (73.1, 86.6)
12 months	NE (NE, NE)	79.9 (73.1, 86.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.60	3.32

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	9 (5.8)	39 (11.6)
Number of Subjects Censored, n (%)	146 (94.2)	296 (88.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.1, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.502 (0.377)
95% CI		(0.717, 3.146)
Log-rank p-value		0.274

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Aspartate aminotransferase increased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.0 (90.2, 97.8)	89.2 (85.7, 92.8)
6 months	94.0 (90.2, 97.8)	85.6 (80.9, 90.3)
9 months	NE (NE, NE)	84.5 (79.4, 89.6)
12 months	NE (NE, NE)	84.5 (79.4, 89.6)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.69	3.42

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	7 (4.5)	39 (11.6)
Number of Subjects Censored, n (%)	148 (95.5)	296 (88.4)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.980 (0.417)
95% CI		(0.875, 4.481)
Log-rank p-value		0.089

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Alanine aminotransferase increased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	95.4 (92.0, 98.7)	89.7 (86.3, 93.1)
6 months	95.4 (92.0, 98.7)	86.7 (82.4, 90.9)
9 months	NE (NE, NE)	84.4 (79.2, 89.5)
12 months	NE (NE, NE)	84.4 (79.2, 89.5)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.73	3.48

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	11 (7.1)	31 (9.3)
Number of Subjects Censored, n (%)	144 (92.9)	304 (90.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.4, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.953 (0.360)
95% CI		(0.471, 1.929)
Log-rank p-value		0.792

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood bilirubin increased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	92.8 (88.7, 96.9)	92.6 (89.7, 95.5)
6 months	92.8 (88.7, 96.9)	88.2 (83.9, 92.5)
9 months	NE (NE, NE)	86.5 (81.1, 91.8)
12 months	NE (NE, NE)	86.5 (81.1, 91.8)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	2 (1.3)	24 (7.2)
Number of Subjects Censored, n (%)	153 (98.7)	311 (92.8)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.576 (0.740)
95% CI		(1.072, 19.530)
Log-rank p-value		0.027

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood thyroid stimulating hormone increased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	98.3 (96.0, 100.0)	93.2 (90.3, 96.0)
6 months	98.3 (96.0, 100.0)	92.1 (88.6, 95.6)
9 months	NE (NE, NE)	89.8 (85.3, 94.4)
12 months	NE (NE, NE)	89.8 (85.3, 94.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.76	3.38

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	8 (5.2)	21 (6.3)
Number of Subjects Censored, n (%)	147 (94.8)	314 (93.7)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.5, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		0.860 (0.429)
95% CI		(0.371, 1.994)
Log-rank p-value		0.713

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood alkaline phosphatase increased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	94.6 (90.9, 98.2)	94.6 (92.0, 97.1)
6 months	94.6 (90.9, 98.2)	92.1 (88.3, 95.8)
9 months	NE (NE, NE)	90.9 (86.6, 95.3)
12 months	NE (NE, NE)	90.9 (86.6, 95.3)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.73	3.61

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	1 (0.6)	18 (5.4)
Number of Subjects Censored, n (%)	154 (99.4)	317 (94.6)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.0, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		7.159 (1.029)
95% CI		(0.952, 53.843)
Log-rank p-value		0.026

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Platelet count decreased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.4 (98.1, 100.0)	94.6 (92.0, 97.1)
6 months	99.4 (98.1, 100.0)	93.7 (90.7, 96.7)
9 months	NE (NE, NE)	93.7 (90.7, 96.7)
12 months	NE (NE, NE)	93.7 (90.7, 96.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.55

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	4 (2.6)	15 (4.5)
Number of Subjects Censored, n (%)	151 (97.4)	320 (95.5)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (3.55, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		1.360 (0.570)
95% CI		(0.445, 4.158)
Log-rank p-value		0.620

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Blood creatinine increased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	97.7 (95.1, 100.0)	95.3 (92.9, 97.7)
6 months	92.8 (83.2, 100.0)	94.4 (91.4, 97.4)
9 months	NE (NE, NE)	94.4 (91.4, 97.4)
12 months	NE (NE, NE)	94.4 (91.4, 97.4)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.73	3.68

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	1 (0.6)	10 (3.0)
Number of Subjects Censored, n (%)	154 (99.4)	325 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		4.345 (1.050)
95% CI		(0.555, 34.013)
Log-rank p-value		0.128

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Amylase increased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Kaplan-Meier Estimates at % (95% CI)		
3 months	99.3 (98.0, 100.0)	96.7 (94.7, 98.7)
6 months	99.3 (98.0, 100.0)	96.7 (94.7, 98.7)
9 months	NE (NE, NE)	96.7 (94.7, 98.7)
12 months	NE (NE, NE)	96.7 (94.7, 98.7)
18 months	NE (NE, NE)	NE (NE, NE)
Median Follow-up Time (months)	2.79	3.58

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.

Table 35.1.1.6.1.3O
Summary of Time to Onset of TEAE by SOC/PT by Liver Metastases
Safety Population
TEAE in SOC Term **Investigations** and Preferred Term **Lipase increased**
Yes

Statistics	Placebo + BSC N=155	Fruquintinib + BSC N=335
Number of Subjects with Events, n (%)	2 (1.3)	10 (3.0)
Number of Subjects Censored, n (%)	153 (98.7)	325 (97.0)
Time to first TEAE (months)		
25% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Median (95% CI)	NE (NE, NE)	NE (NE, NE)
75% percentile (95% CI)	NE (NE, NE)	NE (NE, NE)
Min, Max	0.4*, 6.8*	0.6*, 17.5*
Comparison (Fruquintinib + BSC vs Placebo + BSC)		
Hazard Ratio (SE)		2.153 (0.776)
95% CI		(0.471, 9.841)
Log-rank p-value		0.309

* indicates censored value.
Note: The adjusted HR and its 95% CI are estimated using unstratified Cox's proportional hazards model in which the randomization schedule stratification factors and treatment group are covariates.
P-value is calculated using the stratified log-rank test.
Follow-up time (months) is calculated as ((last dose date + 37 days) – first dose date + 1)/30.4375.
Note: Percentages are based on the number of subjects in each treatment group unless otherwise specified.
BSC=Best supportive care; CI=Confidence interval; HR=Hazard ratio; Max=Maximum; Min=Minimum; SE=Standard error.